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SYDNEY, SATURDAY, MARCH 30, 1929.

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BACTERIOPHAGE IN ITS CLINICAL ASPECTS.<sup>1</sup>

By F. M. BURNET, M.D. (Melbourne), Ph.D. (London),  
(From the Walter and Eliza Hall Institute of Research,  
Melbourne.)

BACTERIOPHAGE phenomena have become of general interest to bacteriologists only in the last six or seven years, although the fundamental discoveries were made in 1915 and 1917. The subject is now mentioned in most text books, but the work is so recent that it is probably advisable to describe briefly the history of their discovery and the general nature of the phenomenon before considering their possible relationships to the processes of bacterial disease.

There is no question that the priority in the discovery of bacteriophage belongs to the English bacteriologist Twort whose work was published in 1915. But this paper failed to attract attention until after the publication of d'Herelle's monograph in 1921. d'Herelle's work was independent of Twort's and was primarily concerned with a much more striking example of bacteriophage activity than the latter's. It was his monograph and particularly the claims made therein as to the importance of bacteriophage in enteric and other infections that caught the attention of bacteriologists and resulted in the great mass of work that has since been done on the subject. It will be convenient, therefore, to approach the subject from the same angles as d'Herelle by giving a short description of his first observations.

d'Herelle had during 1912 observed irregularities in cultures of a certain cocco-bacillus responsible for an epidemic intestinal disease in locusts. Over certain small areas of agar cultures the bacteria were apparently unable to grow. He regarded these appearances as possibly caused by some invisible microorganism whose presence inhibited bacterial growth. On the analogy of hog-cholera in which it has been shown that two agents are concerned, one a filterable virus, the other a paratyphoid-like bacillus, d'Herelle made experiments to see whether the hypothetical invisible microorganism that caused the cultural irregularities might not be the primary invader in the locust epidemic, preparing the way for the subsequent attack of the cocco-bacillus. These experiments gave no definite results, but left him with a sense of the possibility of such filterable viruses being concerned in many enteric infections.

Following out this possibility in the case of dysentery in man due to Shiga's bacillus, d'Herelle examined the effect of adding bacteria-free filtrates made from the stools of dysentery patients to cultures of the bacillus. Acting on the supposition that a virus responsible for the human disease was being sought for, most of the filtrates were naturally made from the stools of patients early in the disease. These showed no particular effect in modifying the

cultural or infective characteristics of the bacilli, but with a filtrate of the faeces from a patient at the beginning of convalescence a striking result was obtained. A drop of the filtrate was added to a young broth culture of Shiga's bacillus and the mixture incubated. After three or four hours the normal turbidity of the growing culture began to diminish and the broth soon appeared perfectly limpid. Microscopically no formed elements could be seen and subcultures on agar showed that no living bacteria were present.

If a minute amount of this cleared broth culture or a filtrate prepared from it was now added to a fresh culture of the dysentery bacillus, even as little as one-millionth of a cubic centimetre, the same clearing occurred after a few hours' incubation. The effect was in this way indefinitely transmissible from culture to culture and at once suggested the theory that d'Herelle has since upheld, namely, that a filterable virus was present parasitic on and multiplying at the expense of the bacteria.

On solid media the effects of the agent were equally striking. If an agar plate was spread with a few drops of a young culture to which undiluted filtrate had been added, no growth occurred or at most one or two resistant colonies developed. If before being added to the broth culture the filtrates were diluted to give a succession of tenfold dilutions, platings showed that at a certain dilution fragments of culture developed with a characteristically worm-eaten appearance.

With still further dilution of the filtrate plates prepared from the mixture showed a uniform layer of bacterial growth scattered over which were isolated circular areas completely free from growth. The number of these clear areas or plaques was strictly proportional to the amount of filtrate added to the culture.

The figures reproduced show two typical examples of this effect. The phages used differ from one another in the size of the plaques produced, that shown in Figure I giving areas of clearing nearly a centimetre across, while the second gives much smaller zones, a millimetre in diameter or less.

Entirely similar phenomena can be observed if other of the pathogenic intestinal bacilli and appropriate faecal filtrates are used. It is not so easy to obtain phages lysing other groups of bacteria, but if sufficient search be made, they may be obtained active against most other pathogenic bacteria. Undoubted phages showing (sometimes in slightly modified form) the cardinal properties of indefinitely transmissible lytic action, filterability and the formation of plaques on agar have been recorded lysing the diphtheria bacillus, haemolytic and faecal streptococci, meningococci, staphylococci, the cholera vibrio, *Bacillus pestis* and other pasteurellas, several of the plant pathogens and the root-nodule bacteria of the *leguminosae*.

To account for these phenomena d'Herelle assumed that there was present in the faecal filtrates a particulate ultramicroscopic virus capable of living as a parasite in the Shiga bacillus and

<sup>1</sup> Read at a meeting of the New South Wales Branch of the British Medical Association, together with the Section of Hygiene and Preventive Medicine and the Section of Pathology and Bacteriology on September 27, 1928.

multiplying at its expense. This virus he called the bacteriophage. The name or its shorter form, "phage," has now passed into general use for these phenomena, although a few authors still use the more non-committal term of transmissible microbic autolysis.

The process of lysis in d'Herelle's view, then, is somewhat as follows. The virus particle when it comes into contact with a sensitive bacterium, is specifically adsorbed to its surface. It penetrates into the bacterial substance and there multiplies, producing from six to sixty descendants and eventually disrupting the organism. With this disruption or lysis the virus particles are set free and become capable of continuing the process as soon as they come into contact with further sensitive bacteria. In a broth culture this proceeds until the whole of the sensitive bacteria present is destroyed. On an agar surface the successively liberated phage particles can naturally only lyse those bacteria in the immediate vicinity. Lysis therefore results in a circular area of clearing that slowly extends as long as the bacteria are actively growing.

The theory of d'Herelle provoked a good deal of opposition initiated by Bordet and developed by German authors who held that bacteriophage lysis was not due to an independent virus, but was a manifestation of some disequilibrium

within the bacterial cell that resulted in autolysis. Nowadays it is admitted that the agent respon-

sible is particulate, but there is no general agreement as to its biological nature. On the whole unbiased opinion leans to the view that the virus theory of d'Herelle allows the clearest description of the facts at present available and that discussion of the intimate nature of the agent may be deferred until knowledge of the other virus diseases advances far enough to allow a wider view of the whole problem of the nature of the filterable viruses.

Without going into details it may be stated that the analogies between bacteriophage, the viruses of the plant mosaics and of the Rous tumours of fowls are very striking. It seems almost certain that biologically similar processes are at work in these three cases. In all three there are hints that the organism affected may itself be primarily responsible for the appearance of the infecting agent, but at present the only way to avoid being tangled in unlikely hypotheses is to consider the agent in each case as an independent ultra-microscopic virus.

The phenomena *in vitro* are amongst the most dramatic in the sphere of bacteriology and at the time of their discovery held out a prospect of an amazing revolution in the therapy of infective bacterial disease. In bacteriophage there seemed to be

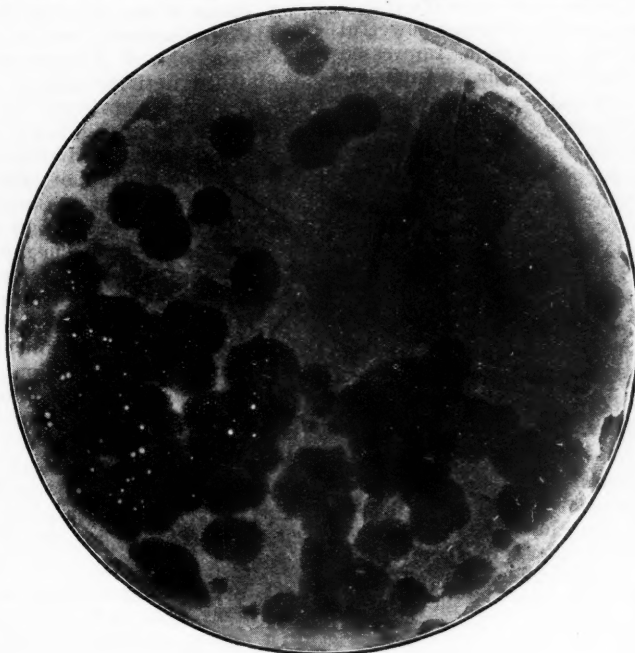


FIGURE I.  
A large-plaque bacteriophage.

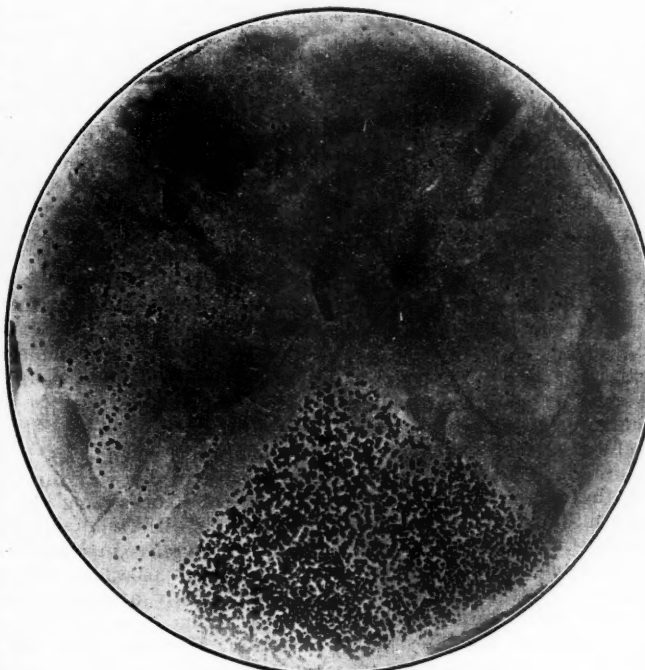


FIGURE II.  
A small-plaque bacteriophage developed on the same organism as that shown in Figure I.

the ideal antiseptic for dealing with bacteria within the body. It was an agent without any effect on the tissue cells, specifically destructive for the invading organism and becoming more and more powerful as destruction of the bacteria proceeded. Impressed with these possibilities d'Herelle made an intensive study of bacillary dysentery and some other diseases to determine the part played by phage in normal recovery and its possible therapeutic applications.

From his results with bacillary dysentery due to Shiga's bacillus d'Herelle drew the following conclusions.

1. That convalescence appeared as soon as an active bacteriophage was present in the intestinal tract.

2. That in fatal infections no bacteriophage active against the invading strain in the intestinal contents could be demonstrated.

3. That administration of a highly active phage invariably cured Shiga dysentery within forty-eight hours.

No one has yet confirmed these findings as a whole, although many reports of clinical successes by the administration of phage have been published. There have been equally frequent reports of the failure of treatment by bacteriophage, but in most of these it may be doubted whether the phage used was as active as is necessary for successful therapeutic use.

At present it does not seem possible to assess the importance and therapeutic value of phage in bacillary dysentery, but at least a case has been made out for the importance of the study of phage in relation to infective disease in general.

Without accepting the sweeping conclusions of d'Herelle, we can nevertheless feel fairly confident that an agent showing such striking effects *in vitro* must have some effect on the course of an infection by a bacterial species sensitive to its action. Some of the aspects of bacteriophage phenomena that seem to have a bearing on the disease process may, therefore, be discussed.

In the first place there is the question of the origin of the bacteriophage. It may be taken as proved that in the great majority of intestinal infections, dysentery, typhoid fever and so forth, a phage active against the infecting organism is present in the intestinal contents at some period of the disease.

Some authors, particularly Bordet, see this appearance of phage as the result of an effect of the body defences on the infecting bacterium inducing a metabolic vitiation that manifests itself in the bacteriophage phenomenon, but if we accept the virus theory, we must assume with d'Herelle that all bacteriophage is derived from preexistent bacteriophage. Now it is found that the faeces of normal animals almost invariably contain bacteriophage active against one or other of the intestinal organisms. In man phages lysing certain strains of *Bacillus coli* are most frequent, but in the horse and the fowl highly active Shiga dysentery phages are very commonly present. Presumably such phages are living at the expense of the coliform

bacilli or other normal inhabitants of the intestinal tract.

A phage is not necessarily limited in its action to the one bacterial strain or species on which it has been isolated. Usually it will show a somewhat diminished activity against several other strains. As an example, one of the phages with which I have worked was originally isolated from the faeces of a fowl and lysed *Bacillus dysenteriae* Shiga actively. If a drop of this phage undiluted was plated with a strain of *Bacillus enteritidis* Gärtner only a dozen or so plaques appeared, although on the homologous organism the same amount of phage suitably diluted would have given several million clear areas. A broth culture of this Gärtner strain was inoculated with material from the centre of one of the few plaques which developed on that organism. After incubation the culture cleared and was shown to contain a phage that lysed both the Shiga and Gärtner strains with approximately equal activity. This result exemplifies, first that a single phage may be active against two or more bacterial species and secondly that an originally weak phage may become much more active after it has been grown at the expense of some new organism.

It is easy to see from such results that, when infection results in the appearance of large numbers of a new potentially sensitive bacterial species in an alimentary canal containing phage normally propagated on *Bacillus coli*, this phage may readily give rise to a modification more active than the original against the pathogenic form. There seems to be no necessity to assume any other mechanism for the appearance of specifically active phages in the course of the various forms of enteric disease.

Closely related to this power of adaptation to a new substrate organism is the question of the increase in virulence of phage. Phage virulence is rather difficult to define, but increase or decrease of virulence is easily recognized in any given case. As a phage becomes more virulent, one finds that it clears a broth culture more rapidly and that the culture then remains clear for a longer period before resistant organisms develop. The number of particles present on the completion of lysis is greater with the more virulent phage.

If a phage obtained in the usual way from a faecal filtrate is grown on the sensitive organism in broth, filtered when lysis is most nearly complete and carried in this way through a series of passages on the one organism, its activity is usually increased. d'Herelle suggests that an almost indefinite increase in virulence may be obtained by very frequent passage, but in my experience the activity quickly attains a certain level and thereafter remains more or less unaltered by further passage. However, with Shiga strains and with some staphylococci it is possible to obtain phages of what d'Herelle terms maximal activity, that is a broth culture of the sensitive organism lysed by phage remains perfectly clear, no matter how long it is incubated.

If phage is to be used therapeutically, it is naturally advantageous to use one of the greatest available activity and d'Herelle is probably justified in demanding that phages of maximal activity only should be used when one is trying to determine the therapeutic efficiency of phage in any given disease. He states that by using weak phages the infecting organism is enabled to develop a resistance against subsequent attack by stronger phages and with this resistance becomes more pathogenic. On this view the administration of a moderately active phage is liable to be positively harmful, but there is very little evidence to support the contention. All that is available goes to show that resistant cultures derived from normal virulent strains have a diminished pathogenicity. In fact, a large proportion of resistant cultures are in the so-called rough state and are almost completely devoid of pathogenic action. This is supported by the fact that although phages of all degrees of activity have been administered to patients with intestinal infections, no one has reported any harmful effects.

The origin of resistant cultures after lysis is a complicated and extremely interesting question, but it seems fairly certain that they play no important part in disease. Failure of phage to induce therapeutic results cannot be attributed to the appearance of these resistant bacteria.

It is much more likely that the reason why reactions in the infected body are much less striking than those in the test tube lies in the nature of the medium in which the bacteria are growing and in which lysis takes place. In a broth culture the bacteria are actively growing, they are (if motile) moving freely about and in any case are liable to free chance contact with any phage particles present, under the influence of convection currents, Brownian movement *et cetera*. In addition there are no foreign colloidal substances present to adsorb the phage particles or otherwise to hinder their action. In the body, however, bacteria are usually present in relatively small numbers (compared with the numbers in broth cultures) and when in the tissues are multiplying in complex colloidal systems where there is little freedom of movement. When the infection involves a surface exposed to the environment, either external or internal, as in the alimentary tract, there are as well as the invading organisms millions of more or less saprophytic bacteria present in the same medium.

All these factors will tend to reduce the activity of phage within the body. The experimental evidence for each of these effects may be briefly mentioned.

In the first place certain colloids of which gelatine is the best known example, actively inhibit the processes of lysis. In 5% gelatine broth no visible lysis will occur, although some multiplication of the phage may take place. Incubated at a suitable temperature plates of solidified nutrient gelatine show no formation of plaques or any other evidence of phage activity, although at the same temperatures plaques are well shown on nutrient agar. Serum

shows a similar but less evident effect. The nature of the inhibitory action is not yet settled, but the evidence seems to favour Bronfenbrenner's view that the phenomenon is related to the power of certain emulsoid colloids to prevent or diminish imbibition of water from solutions containing them. One of the stages of bacterial lysis seems to depend on imbibition of water from the surrounding medium. If this is prevented, lysis and consequent liberation of further phage cannot go on.

In the second place pathogenic bacteria in the body are in a relatively unfavourable medium for multiplication. The defences of the body are actively directed against them and only in overwhelming infections does there appear to be anything like free multiplication within the body. Now *in vitro* it is invariably found that, other things being equal, anything that diminishes the activity of multiplication of bacteria, diminishes phage activity. No lysis takes place when phage is added to suspensions of bacteria in saline or other non-nutrient medium and in general active multiplication of phage in broth cultures takes place in the period when bacterial growth would normally be most active. Traces of antiseptic in the medium insufficient to stop bacterial growth completely, generally inhibit the multiplication of phage even more.

In the third place bacteriophage is specifically adsorbed to bacteria sensitive to its action, but also though to a much smaller extent to other bacteria and to many non-living adsorptive agents. Electro-positive surfaces are particularly effective, for example, if a phage is filtered through a plaster of Paris filter, the filtrate shows no activity whatever. The particles have all been adsorbed to the oppositely charged surface. It can be seen, therefore, that in, say, the intestinal contents of a patient with acute dysentery, there are many ways in which the activity of bacteriophage might be greatly lessened by such adsorptive processes.

All the factors that have been described as likely to diminish the activity of phage in the infected body, are purely relative, but taken together they make the observed failure of phage to influence most intestinal infections more readily understood.

It is, of course, possible that lysis of only a very small proportion of the pathogenic bacteria present might be sufficient to alter the balance in favour of the body, but on general grounds the only diseases in which good results by the direct activity of phage are to be expected, are those in which the infecting organism is localized in some body cavity rather than in the tissues and of which the microorganism itself is highly susceptible to lysis. The human diseases that most adequately fulfil these requirements, are Shiga dysentery and Asiatic cholera and it is significant that these two diseases are the only ones in which at all well substantiated therapeutic effects have been obtained.

Work on the significance of bacteriophage in cholera is apparently being actively pursued at present in India, but I have seen only preliminary

reports of the work so far. Malone and d'Herelle are claiming a wide epidemiological significance for cholera phages. They find them present in well and surface waters in the endemic regions and consider that they play a predominant part in natural control of the disease. Therapeutically they claim that administration of phage resulted in a mortality of 8% among 69 patients, while of 73 controls treated by other methods 77% died. These results have been confirmed in a small series treated by Ross, Bagchi and Roy who encountered only two deaths among sixteen patients treated with an active cholera bacteriophage.

The matter, of course, needs much more confirmation, but *a priori* the very fluid intestinal contents of a cholera patient would seem to offer a very close analogy to test tube conditions and thus allow an active phage to reduce rapidly the number of vibrios present.

#### Conclusion.

It is impossible to make any broad statements as to the importance of bacteriophage in disease. Each type of infection must be separately considered and even if this is done, the evidence is frequently contradictory and a valid judgement impossible. However, we may state as the most reasonable view possible at present:

1. That in the diseases which are essentially or largely septicæmic, phage plays little part and can be of therapeutic use only indirectly owing to its content of associated bacterial antigens. Such are plague and typhoid fever.

2. That in infections practically limited to the contents and lining of the alimentary canal such as bacillary dysentery, food poisoning by the Salmonella group and cholera, a phage active against the pathogen usually develops and may play a part in determining recovery. In this group the administration of active phage by mouth is a rational therapeutic procedure and although there is no unanimity of opinion on the point, it seems to have been responsible for some extremely successful results.

#### RECENT ADVANCES IN IMMUNIZATION.<sup>1</sup>

By E. L. MORGAN, M.B., Ch.M.,

Principal Microbiologist, Department of Public Health,  
New South Wales.

WHEN asked to speak on recent advances in immunization, I was confronted with so wide a subject that I have decided to confine my remarks to recent advances in certain infectious diseases which are prevalent in Australia.

The diseases I propose to discuss are typhoid fever, poliomyelitis, scarlet fever and measles.

The list is necessarily incomplete. The recent tragic happening at Bundaberg has already focused the attention of the medical profession on the

methods of prevention of diphtheria, so that I do not propose further to discuss this disease.

#### Typhoid Fever.

The usual method of immunization against typhoid fever by subcutaneous injection is so well known as to require little comment. I propose, however, to discuss the administration of vaccine by the mouth as advocated by Besredka.

Rabbits are extremely resistant to massive doses of typhoid or paratyphoid bacilli given by the mouth, but Besredka found that when bile was administered this immunity was broken down. He points out that bile favours the growth of typhoid and paratyphoid bacilli in the intestine and it has a desquamating effect upon the epithelium, enabling the bacilli to lodge there, multiply and invade the organism. The lesions produced by the administration of typhoid bacilli are confined to the intestine, whether the organisms are administered orally, subcutaneously or intravenously. If bile is given, however, the required dose is reduced, for example, after administration of bile, one-fifth to one-tenth of the intravenous dose of those organisms will produce disease.

Besredka then showed that if two rabbits which had been fed equally on living and dead cultures of paratyphoid bacilli, were given a lethal dose of similar organisms intravenously, the rabbit that had been given bile along with the bacilli, lived, while the other died. Immunity produced in this manner is established in three days as against ten to fourteen days in the case of the subcutaneous method. This immunity is not dependent on the amount of antibodies in the serum, as ingestion of typhoid bacilli produces antibodies in the blood whether the animal has been sensitized with bile or not. Antibodies in the blood, however, are not parallel with immunity, as in the course of immunization by the mouth the antibodies gradually disappear from the blood, yet the rabbit is immune to typhoid fever. The work of Burke and Barnes tends to confirm some of Besredka's observations with regard to the production of agglutinins in the blood by oral administration and their experiments also suggest that the methods by which the vaccine was prepared, may possibly affect the immunity response. Although the conclusions of Besredka have not been generally adopted, several favourable records of oral immunization against typhoid fever have been published.

Dr. Gauthier administered typhoid vaccine by the mouth to 1,200 people in a town where typhoid fever was endemic; none developed the disease during the succeeding six months. He next tried oral administration in two towns where epidemics of typhoid had broken out. One cubic centimetre of vaccine was given for three consecutive days and after seven days no further cases occurred. In South Africa Boyd reports that no case of typhoid following oral immunization occurred amongst 2,386 persons (922 Europeans and 1,464 coloured persons). He also suggests that the vaccine thus

<sup>1</sup> Read at a meeting of the New South Wales Branch of the British Medical Association on September 27, 1928.

administered may eliminate the bacilli from carriers.

Vaillant deals with an epidemic in the devastated region of the Pas de Calais. Injection was first tried, but the inhabitants of most of the villages refused to continue with injections on account of the severity of the reactions. Oral administration was resorted to. On rising after fasting typhoid, paratyphoid A and B vaccine was given by the mouth, together with a bile pill for three consecutive days or for two days in children under seven years. No untoward reactions attributable to the vaccine resulted. The results were remarkably successful. Among 600 to 650 non-vaccinated persons the incidence was 50 cases (about 7.7%); among 173 vaccinated by typhoid, paratyphoid A and B injection, four cases (2.3%). Among 1,236 inoculated by the mouth with bile vaccine there were two cases (or 0.17%). The figures make allowance for persons vaccinated during the incubation period.

Certain slight sources of error are mentioned and the results on the figures are perhaps slightly more in favour of oral vaccine than they should be, as the inhabitants of the most severely infected village submitted to hypodermic injection.

Originally the standard strength of typhoid vaccine as issued by the Health Department was one thousand million per cubic centimetre of mixed *Bacillus typhosus*, *Bacillus paratyphosus A* and *B*. At the end of the war it was decided to adopt the British Army standard of two thousand five hundred million per cubic centimetre. Unfortunately, vaccine of this strength produces fairly severe reactions and though the resulting immunity may be greater than that produced by the earlier vaccine, there is no doubt that people often object to the injection on account of the severity of the reaction.

I understand from Dr. Heiser that in India when both oral and subcutaneous methods were tried, the native population strongly opposed the oral method and preferred the injections.

The oral method does not appear to produce the discomfort so often associated with injection and most of the published reports of its application are undoubtedly favourable, so it may yet come to replace the older method, though before discarding the latter it is well to consider that it is a tried and proved method with which the public is familiar.

#### Poliomyelitis.

In poliomyelitis the use of serum therapy is not so much aimed at checking the spread of the disease as at curtailing the effects of the disease, once it is definitely diagnosed. It may be denied that the administration of serum has any decided value, but it has been proved in other diseases that the serum of recovering patients is frequently rich in antibodies. Experimental work in poliomyelitis strongly indicates that human convalescent serum is a specific in producing prompt recovery and in preventing paralysis, if given in the preparalytic stage. Further, if given after the commencement of

the paralytic stage, it limits the spread, though it does not appear to aid the disappearance of already established paralysis.

The plan adopted in Melbourne to deal with the outbreak in 1925 is more comprehensive than any measures so far adopted in this State. In Melbourne a committee was formed representing the Melbourne City Council and the metropolitan municipalities and this committee appointed a special medical officer to take charge of the activities for dealing with the outbreak. The expenses were borne half by the participating municipalities and half by the State Government. Full details of the early work have already been published. Serum from convalescent patients was collected and graded according to the date at which the patient suffered from the disease. This was issued at the direction of the medical officer in charge. The serum was administered intrathecally, intravenously and subcutaneously. The largest amount given intrathecally was thirty cubic centimetres and the average amount of serum administered to each patient was about fifty cubic centimetres. No untoward reactions attributable to the serum were noted. Recently the scope of the work has been extended. Specially trained consultants have been appointed at various centres. These consultants attended an intensive post-graduate course dealing with poliomyelitis in all its aspects and subsequently supplies of serum were made available for use under their supervision. The cooperation of the hospitals has also been obtained.

While it is alleged that the Melbourne organization is far from perfect, the scheme embodies the main principles of definite diagnosis of cases and controlled issue of serum which must eventually lead to the achievement of better results in the treatment of poliomyelitis.

A limited amount of serum was made available in 1926 by the New South Wales Health Department, but there has been no demand for it and it is practically impossible to maintain fresh supplies of serum in the absence of an epidemic. Further, the diagnosis must be undoubted before the use of serum appears to be justifiable and unless some such scheme as that in operation in Melbourne is started in this State, results of value are not likely to be achieved.

#### Scarlet Fever.

Modern methods of control of scarlet fever have largely followed on the work of Dr. George and Dr. Gladys Dick. Prior to the publication of their work there had been others who advanced the theory that scarlatina is caused by streptococci, but it was not realized that only certain individuals are susceptible, nor was it generally accepted as definitely established that symptoms akin to scarlet fever can be produced by injection of an exotoxin of certain streptococci. A small percentage of streptococci capable of producing this toxin has been isolated from a number of other conditions as well as scarlet fever, while by no means all the streptococci isolated from scarlet fever patients are capable

of producing this toxin. At first sight these facts suggest a lack of specificity on the part of the streptococci in relation to scarlet fever. The evidence on this point, however, is so overwhelming as to leave no reasonable doubt as to their causal relationship to the disease.

Schultz and Charlton had found that the intracutaneous injection of serum from a patient recovering from scarlet fever would cause blanching of the rash. Further, they ascertained that serum from certain healthy members of the community would produce the same phenomenon, while the serum of others would not do so.

The Dicks also showed that an antitoxin could be made which would neutralize the effect of the exotoxin, and also would produce the same blanching of the scarlet fever rash as Schultz and Charlton had observed with convalescent serum. Further, when a suitably diluted toxin is injected into the skin, a certain number of individuals will develop a reaction at the site of injection, while others will not do so. This reaction is now known as the Dick test, a test by which we are largely able to determine those who are or are not susceptible to scarlet fever.

When a large dose of toxin is injected into susceptible individuals, symptoms similar to a mild attack of scarlet fever develop and following on this a large percentage of those individuals proves to be immune to scarlet fever. However, unlike the immunity produced by a mixture of diphtheria toxin and antitoxin, the immunity does not appear to be permanent, the majority of individuals again becoming susceptible after a period of about nine months. Smaller doses of toxin will produce immunity, but experimental work appears to indicate that the immunity is more lasting when a good reaction is produced.

Those persons immunized in this way as well as those with acquired immunity do not react to the Dick test.

A very transient immunity can also be produced in a susceptible person by the injection of scarlet fever antitoxin. Unfortunately passive immunity is of extremely short duration, lasting about ten days to three weeks, but it is well to remember that even such transient immunity may be very useful in checking an outbreak of scarlet fever in an institution.

By the application of these principles we are now able to plan methods of controlling outbreaks of scarlet fever occurring under varying circumstances. In planning control measures two important points arise: (i) the incubation period of scarlet fever and (ii) the period of infectivity of a patient.

#### *The Incubation Period.*

I personally am of opinion that the incubation period is under seven days, although I am aware that many experienced writers claim a longer incubation period. This point is important because on it largely depends the control of an outbreak by passive immunization.

With regard to the infectivity of a patient I will quote W. Arnold:

One may say that scarlatina is a moderately infectious disease for two weeks after the onset, but that the majority of cases cease to be infectious some time during the second fortnight, so that at the end of the fourth week only a small percentage remains so. Out of this small percentage some, including some mild cases, probably remain infectious for several months, though they are not recognizable by any known method; it is possible a still smaller number retain the power of infecting for a much longer period, perhaps even so long as a year.

Using the facts enumerated above, we can give consideration to the methods of control of a scarlet fever outbreak in, say, a school or a hospital. By means of the Dick test the susceptible individuals are ascertained and then immunized.

If the outbreak has occurred in a hospital, passive immunization may be the most suitable procedure to adopt. The patients are under medical supervision and any reaction attributable to the serum can be treated immediately. If the outbreak has occurred in a school, active immunization is the method of choice. It takes about three weeks for immunity to develop and during this period the question of excluding the treated children from school could be considered.

With regard to private patients it would be well to immunize the family while the patient is in hospital, so that there should be no susceptible contacts when the patient returns home.

Several interesting points appear in most of the reported series of immunizations.

1. Although an attack of scarlet fever produces immunity, a considerable number of individuals who have had the disease, still give positive Dick reactions.

2. Amongst the negative Dick reactors occasional cases of scarlet fever develop.

3. The extraordinary range in the number of skin test doses of antitoxin used by different workers in producing immunity. While the average appears to be from 250 to 5,000, I have seen records of one skin test dose producing immunity, while at the other end of the scale amounts ranging up to 60,000 skin test doses do not invariably produce immunity.

4. By no means all who receive prophylactic doses of toxin, develop immunity. The number who do develop immunity, appears to vary from 50% to 90%.

While occasionally it must be very disappointing to a parent who has had a child tested by the Dick test and then immunized, to find that the child develops scarlet fever, there is no doubt that by the application of the principles I have outlined, outbreaks of scarlet fever can be largely controlled.

#### **Measles.**

Measles is perhaps the most recent disease to be attacked on a large scale by the immunologist. At the same time the methods in vogue can hardly be said to be new, as they were apparently first suggested by Alexander Munro in 1757 and in 1759 Francis Home is known to have carried out active

immunization against measles. During recent years the medical profession in England has gradually come to regard measles in young children as a more serious disease than scarlet fever. Dr. Copeman states that the Metropolitan Asylums Board has recently been giving preference to measles over scarlet fever in the wards of their hospitals. Of all deaths from measles 70% occur in children under three years of age, so in formulating any plan of campaign for the control of this disease it is obvious that it must be directed at reducing the incidence in this age group.

If measles were to be completely eradicated from any nation, it is more than likely that any inherited resistance to the disease would die out and gradually the race would become highly susceptible; accidental introduction of the disease might then practically decimate the population. Previous similar tragedies have shown that such a catastrophe can occur. The prevention of every case of measles is, however, not a practicable proposition. Few healthy children over the age of five die from measles, so methods of control must be largely directed at warding off the disease till the child has reached that age.

It is now known that the serum of convalescents and to a less degree the serum of adults who have had measles during childhood, may be employed with a view to producing immunity. Instead of serum, citrated whole blood can be employed, necessarily in larger quantities. The results from injection of serum vary according to the condition of the patient at the time of administration.

1. In ordinary circumstances injection of serum produces passive immunity which lasts for about one month, and a similar result follows if given during the first five to six days of the incubation period. It has been noted, however, that the later the serum is injected, the larger will have to be the dose.

2. If serum is injected after the sixth day and before the ninth day of the incubation period, no amount, however large, will prevent the attack. Modified measles will develop and an active immunity results.

3. If the serum is injected later, about the tenth day, the course of the disease is unaffected, but an area of local blanching of the rash will occur—the phenomenon of Depré.

4. If serum is injected later than this, no apparent action is noted and the disease runs its course.

5. If serum is injected into an unaffected individual and this is followed by the injection of virus (blood from a person with an early attack of measles), active immunity results.

The modified disease mentioned in the second method is characterized by absence of catarrhal symptoms, Koplik spots and high temperature with a diminished rash and fewer complications. This is the result which is most likely to be of value in producing permanent immunity, but it is also claimed that by the fifth method an immunity can be produced which is likely to be permanent. Dif-

ferent workers vary slightly in their recommendations as to dosage, but a range covered by three cubic centimetres for a child aged three and ten cubic centimetres for a child aged ten would include practically all the recommendations.

Before closing the subject of measles, I would like to mention that Tunncliffe in America produced strong evidence that a green producing diplococcus was the causative organism of measles. Park, however, was unable to obtain the same results. Should the causal nature of this organism be definitely established, it will go a long way towards solving the problem of obtaining adequate supplies of serum.

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#### SCARLET FEVER.<sup>1</sup>

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THOUGH primarily intended for the Sections of Public Health and Pathology and Bacteriology, I shall endeavour to make this short contribution of interest to the general practitioner, because he is the first line of defence against infective diseases not excluded by quarantine and his efficiency and cooperation are essential if ever we take up the offensive against scarlet fever. I propose to show that there are two problems in connexion with this disease, the first the administrative public health problem and the second the bacteriological problem. The solution of the former is dependent upon a

solution of the latter. I shall present to you very briefly the public health problem, quoting freely from Parsons<sup>(1)</sup> in his report to the Ministry of Health, the facts and opinions referring, of course, to England and Wales. Though Sydenham published his "*Febris Scarlatina*" in 1676, the name scarlet fever did not come into general use for some time and there was not always a clear distinction in practice between scarlatinal angina and malignant angina (diphtheria). A striking peculiarity in the history of scarlet fever has been its variability in severity (case fatality) at different epochs. For example, towards the end of the eighteenth century it was a very grave disease. Following this period were three decades up to 1830 in which it was a mild infection. "After 1830 scarlet fever rapidly became what it continued to be through more than a generation—the leading cause of death among the infectious maladies of childhood." It is astonishing to look back to 1863 and contemplate a mortality rate of 1,478 per million from scarlet fever alone. Since 1870 the mortality has steadily declined, so that since 1906 it has not been above 100 per million. The case fatality has likewise decreased, for example from 1872 to 1876 it was 12.4% and in 1924 only 1.3%. These remarkable improvements are as difficult to explain as previous fluctuations and they had already well begun before the present era of compulsory notification and treatment in isolation hospitals. It is perhaps too early to come to any definite conclusion as to whether it is a question of an attenuation of virulence of the infective agent or a relative increase in immunity.

With the establishment of isolation hospitals "return cases" became a vexed question. It was found that 80% of infective convalescents suffered from mucous discharges. Long detention in hospital did not reduce the chance of return cases, but local treatment of the throat *et cetera* with transferrine to less infective wards was more promising. The balance of evidence favoured the conclusion "that isolation has not in general influenced greatly either the prevalence or the mortality of scarlet fever." Also "we cannot satisfy ourselves that the discharge of patients from hospital in the late stages of desquamation constitutes a danger to public health." Coincident with these findings after considerable experience of isolation in hospitals are the promising results obtained by home treatment, apparently without any greater danger to the community. Though mortality rates and case fatalities have greatly diminished, the prevalence of the disease has not much diminished since 1911, so that the number of patients to be accommodated in hospitals remains a very large one. But the number of patients "who clinically now require the benefit of hospital treatment form a very small proportion of those attacked." Parsons quotes *The British Medical Journal*<sup>(2)</sup> as follows:

It is now a disease of low mortality and usually of slight severity with a comparatively high degree of infectiousness during the early days of attack, which rapidly subsides, though in exceptional cases it may be indefinitely

<sup>1</sup> Read at a meeting of the New South Wales Branch of the British Medical Association on September 27, 1928.

ILLUSTRATIONS TO THE ARTICLE BY DR. JOHN TANSEY AND DR. LESLIE UTZ.



FIGURE I.  
Showing thyroid gland with substomal prolongation.  
A = attachment to the lung.



FIGURE II.  
Showing sectional view of thyroid gland in Figure I. The arrows indicate the inferior margin of thyroid tissue below which can be seen a secondary nodule.

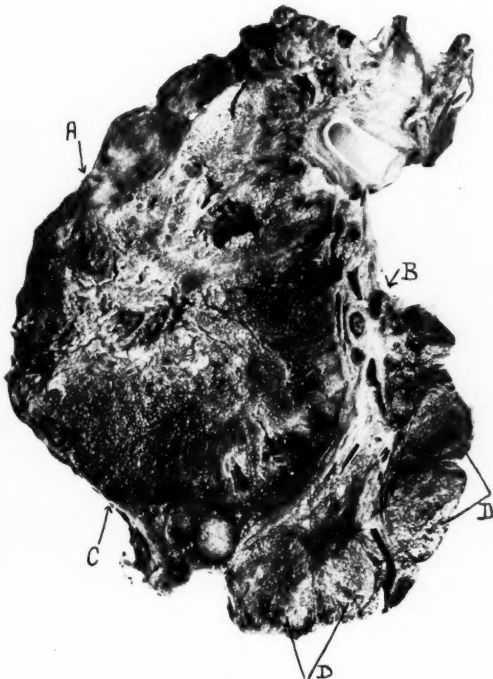


FIGURE III.  
Showing left lung. A marks the very large hæmorrhagic tumour (primary). B and C mark the terminal points of the fibrous band separating the primary from secondary growths. D = secondary nodules.



FIGURE IV.  
Right lung studded by numerous secondary nodules.

ILLUSTRATIONS TO THE ARTICLE BY DR. JOHN TANSEY AND DR. LESLIE UTZ.

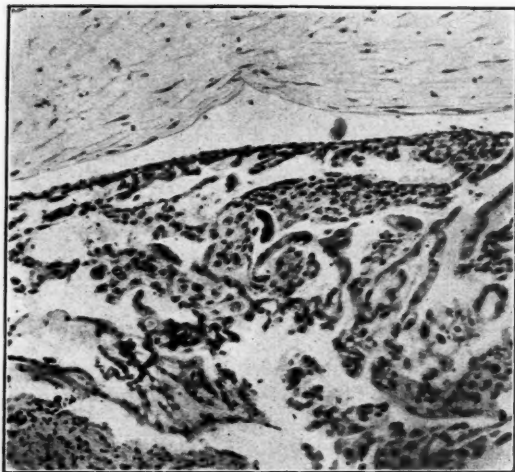


FIGURE V.  
Photomicrograph of section from chorion epithelioma (Dr. D'Arcy's case).

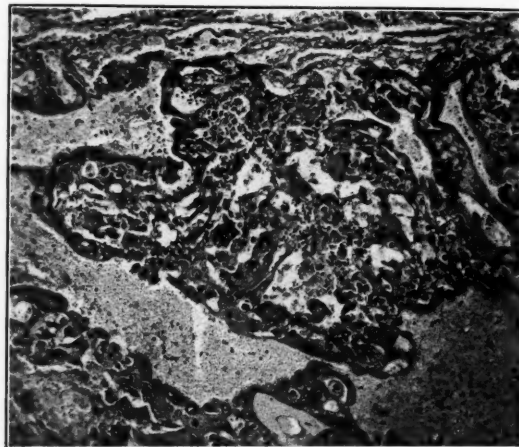


FIGURE VI.  
Photomicrograph of section from primary growth. Note the characteristic syncytial cells and Langhans's cells.

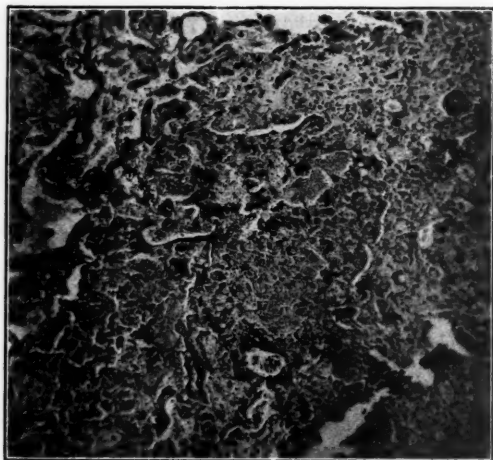


FIGURE VII.  
Photomicrograph of secondary nodule from right lung.

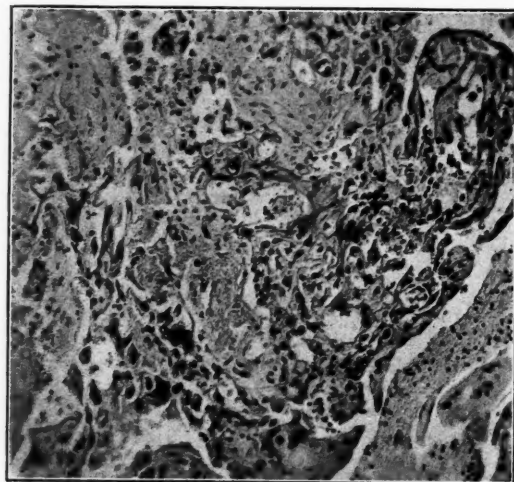


FIGURE VIII.  
Photomicrograph of nodule from chest wall.

prolonged. The measures devised for its control contemplated a disease of serious character, its infectiousness uniform during the period of desquamation, but in the absence of complications ceasing definitely at the end of this period. The change of view which further knowledge has brought, may well be ground for reviewing the whole practice with regard to the preventive measures adopted.

In fact, if there be a shortage of hospital accommodation or if economy is necessary, then the subjects of pneumonia, measles, influenza and *encephalitis lethargica* often have superior claims to hospital treatment over scarlet fever patients. The only special reason for sending scarlet fever patients to hospital is the possibility of preventing the spread of this infection thereby and "on this point at least," says Parsons, "even without the statistical analysis, we may be fairly confident that the argument breaks down."

That eminent authority, Sir George Newman, chief medical officer in the Ministry of Health, throws his weight also in the same publication on the side of a new outlook upon this disease.

As time passes mere isolation seems less important, mere disinfection of the surroundings of the patient less necessary. We cannot, however, say that the principle of isolation can be abandoned, because we are faced with the fundamental and undisputed truth that scarlet fever is an infectious complaint. Nor can we discard disinfection, if, as seems certain, we are dealing with an infection. . . . A vast quantity of popular "disinfection" which goes on at present is not only entirely ineffectual, but wasteful and absurd. To conceal one bad smell by creating another is not disinfection. And, as I have already hinted, we appear to be making substantial advances in our knowledge of the serological circumstances of scarlet fever which may well lead to profound administrative changes in both isolation and disinfection for this disease. There can be little doubt that (a) the proper application of the new knowledge of the relation of ear and throat conditions (one might add nose) to infective processes, (b) the use of barrier nursing, ample cubic capacity and floor space, and open-air treatment in fever hospitals and (c) the adoption of the Dick test and artificial immunity, are likely to contribute to the steady improvement of our whole administrative organization for dealing with scarlet fever. . . . Owing to the mildness of the present type of the disease, many cases are not diagnosed sufficiently early to make their notification and subsequent isolation of much value from a public health point of view. . . . It is to be hoped that notification may become more complete and perhaps more sensitive as a result of the aids to diagnosis which recent bacteriological studies seem to promise. . . . Above all, attention must be given to (i) the strengthening of the resistant powers of the human body, (ii) the direct treatment of all foci of infection and (iii) the large question of immunization, for in these directions we may find an answer to infection much more enduring and effectual than chemical disinfection or steam. Immunization, natural or acquired, is the biological answer to disease.

These administrative problems would be well on the way to solution if we could recognize the infective agent of scarlet fever wherever it might be found, but principally in the throat and nose of man, if we had some practical test for pathogenicity or virulence, if we could free infected persons from this organism, if we could ascertain who is susceptible and who not and if we could immunize those susceptibles who were to be exposed to it. Admittedly a large "if" and involving a large amount of work, but it would probably mean great economy in health and education and in the long

run a saving of expenditure by the State and by parents. This brings us to the bacteriological problem and exceedingly complex though it is, I must hurry more than I would wish.

It was, I believe, Löffler who in 1884 first reported the presence of streptococci in the angina of scarlet fever. Subsequent workers found these organisms so constantly (90% to 100%) that their causal relation was advocated quite early. Russian and Austrian workers were particularly keen on this obvious hypothesis. In fact, the very recent conception of the Dicks<sup>(3) (4) (5) (6) (7) (8) (9) (10)</sup> was anticipated by Savchenko<sup>(11)</sup> who found a toxic substance in streptococcal broth and produced an antitoxic serum. He described scarlet fever as a severe local streptococcal infection accompanied by toxæmia and remarked that it was erroneous to conclude that because the substance was not toxic to animals it was also not toxic to man. Gabrichevsky<sup>(11)</sup> attempted prophylactic immunization in children, using broth cultures and produced general reactions and scarlatiniform rashes. In fact, immunization by vaccines was practised with some success in Russia some years ago. Yet for many years before the work of the Dicks the orthodox view was that the supposed streptococcal aetiology lacked experimental proof and a filter passing virus was suggested. However, much spade work was being done on the streptococci in these years. Streptococci have been classified in various ways, but perhaps their growth on blood agar provides the simplest primary classification (Schottmüller, Smith and Brown). This method defines three groups, the *hemolyticus* which is practically *pyogenes*, *viridans* and *non-hemolyticus*. We are only concerned with the hemolytic streptococci which it is reasonably certain now include the causal agents of scarlet fever, erysipelas, many cases of puerperal fever and many other septic infections in man. Hemolytic streptococci have been found not only in the angina of scarlet fever, but also in the localized septic complications and in malignant cases in the blood during life and the heart's blood after death. Can we differentiate the scarlatinal streptococci from the rest of the hemolytic pyogenes group? According to most authorities neither morphology, cultural characters nor fermentation tests differentiate. Serological tests and mainly agglutination and absorption methods have been vigorously investigated and there have been many hopeful reports based on much laborious work. In particular Dochez, Avery and Lancefield,<sup>(12)</sup> Bliss<sup>(13)</sup> and Tunncliffe<sup>(14)</sup> in America and Gordon<sup>(15)</sup> in England have all reported that the scarlet fever streptococci formed a specific homologous group. Birkhaug<sup>(16)</sup> reported a specific identity for the erysipelas streptococci and Lash and Kaplan<sup>(17)</sup> for those found in puerperal fever. Eagles<sup>(18)</sup> confirmed this work and showed also that during convalescence from scarlet fever the agglutinating titre for the streptococci found progressively diminishes; he suggested that this is an *in vivo* loss of agglutinin due to the action of the antitoxin formed by the patient.

This is a most important suggestion on the problem of the carrier.

Later workers (F. Griffith,<sup>(20)</sup> G. R. James<sup>(21)</sup> and J. Smith<sup>(22)</sup>) rather attack the position of Dochez and others in that they report several groups of scarlatinal streptococci and also heterogeneous strains. J. Smith and his collaborators<sup>(23)</sup> hold that "the same type of streptococcus can on occasion originate at least five separate clinically distinguishable diseases, namely scarlet fever, tonsillitis, erysipelas, puerperal fever and broncho-pneumonia," the disease produced depending on the toxigenic powers of the streptococcus, the susceptibility of the patient and the site of infection.

We turn now to the important remaining character of hæmolytic streptococci, namely, toxin production. Most of the work on this subject is of comparatively recent date and serves to introduce us to George and Gladys Dick whose proof of the ætiological rôle of the scarlet streptococcus has now been widely accepted, at any rate in Great Britain and America. The Dicks have been working for many years in this field, notably assisted by human volunteers for experimental infection. In 1921 they failed to transmit the disease by swabbing the throat with fresh blood serum or filtered throat washings from scarlet fever patients or by subcutaneous injection of their citrated blood or filtered throat washings. Later the throats of thirty volunteers were swabbed with living cultures of hæmolytic streptococci. Seven developed sore throat, fever and leucocytosis, but no rash. Their deliberate conclusion is interesting in view of their subsequent work: "The thirty streptococcal throat inoculation experiments constitute a series large enough to discourage further experiments of the same kind with hæmolytic streptococci." In 1923 a nurse in charge of a scarlet fever patient developed a sore finger and two days later mild scarlet fever. Pus from the finger contained mannite-fermenting hæmolytic streptococci and the Dicks swabbed a culture on to the throats of five volunteers. Three remained well, one developed a sore throat, fever, malaise and cervical adenitis, but no rash and the fifth, a young woman, developed after forty-four hours sore throat, headache, malaise, fever and a rash with subsequent desquamation. Five other volunteers were swabbed with a sterile filtrate of the culture and remained well. Four further volunteers were swabbed with the unfiltered culture and two developed sore throat, one sore throat and a rash with subsequent desquamation. Later on they repeated the experimental infection with a non-mannite fermenting scarlet streptococcus. In 1924 the Dicks described a skin test for susceptibility to scarlet fever, now generally known as the Dick test. This is an erythema at the site of intradermal injection of a high dilution of a toxin produced by growing the scarlet streptococcus in broth or blood broth for variable periods. The toxin is remarkably heat stable and the control injection for detecting pseudoreactions is now made with the same dilution heated for one and a half hours in boiling water

(Zingher). The toxin should be a sterile filtrate and is usually kept carbolized before dilution. During the first few days scarlet fever patients generally give some reaction which usually is not demonstrable at a later stage and may be permanently absent thereafter. There has been more or less confirmation of the Dicks' claims for this test, though some published results, for example, those by Sherwood and Baumgartner,<sup>(24)</sup> have not been as clear cut and other workers have met with irregularities. One suggestion is that a toxin consists of several or many toxic components and that other toxins are not strictly homologous (Ando, Kurachi and Ozaka<sup>(25)</sup>). There are difficulties also in standardization of the toxin owing to the insusceptibility of laboratory animals. However, difficulties are being overcome and the usefulness of the Dick test in scarlet fever control is ably exemplified by the work being carried out with the approval and cooperation of the public health authority in Aberdeen (Kinloch, Smith and Taylor<sup>(26)</sup>). Other points of interest in connexion with this test are that its percentage positivity at different age periods is on the whole comparable with that of the Schick test, reaching a maximum (70%) at one to two years and falling to 17.9% at twenty years and over (according to Zingher<sup>(26)</sup>); also that the toxin is neutralized by most specimens of convalescent serum and horse antitoxic serum; also that in New York children in private schools gave a much higher percentage of positive reactions than the poorer children of public schools.

It is now generally recognized that the high degree of acquired immunity after an attack of scarlet fever is antitoxic only and not antibacterial and this is well borne out by the occurrence of septic complications during convalescence, these being frequently due to hæmolytic streptococci indistinguishable from scarlet streptococci. Perhaps the most convincing confirmation of the Dicks' work has been the production of typical scarlet fever by subcutaneous injection of toxin and this has resulted in very susceptible persons from the injection of not more than five hundred skin test doses. Such a dose, however, usually produces only a local redness, swelling and tenderness and a mild or no general reaction. Active immunization has now been carried out with such promising results in various centres that it is likely to become a well established method in public health and private practice. The question of dosage is a little uncertain and this is partly due to the difficulties of standardization. There is little doubt that the dosage stated in the earlier reports (and they are all quite recent), for example, those of the Dicks themselves, were far too small according to present standards. They have since stated that immunization must continue to the stage when there is no longer a response to the Dick test. The practice of using an initial five hundred skin test doses appears to be growing, although it will admittedly produce general reactions in a small percentage of susceptible people. This is usually followed by one

thousand and three thousand skin test doses at intervals of five to seven days. Others give a fourth injection of five thousand or six thousand doses and maintain that a total of ten thousand to twelve thousand doses is necessary. Others again speak of a total of fifty thousand doses. This question of dosage necessary to abolish a Dick reaction or necessary to produce a high degree of immunity must be considered unsettled. The Aberdeen workers<sup>(23)</sup> have obtained remarkably good results with a dosage of 500, 1,500 and 3,000.

#### Results of Dick Tests in Sydney.

A number of boys at two schools at which a mild epidemic had occurred, were submitted to the Dick test with the following results:

School.	Boys Under 14 Years.			Boys 14 Years and Over.		
	Reaction.	No Reaction.	Reaction.	Reaction.	No Reaction.	Reaction.
A	31	35	% 46.9	48	55	% 46.6
B	53	23	69	33	20	62

School A: Percentage reaction of boys of all ages, average age 14.0 years = 46.7.  
 School B: Percentage reaction of boys of all ages, average age 12.6 years = 66.

A definite difference in the percentage of reactions is disclosed. This may have been due in part to the fact that School A had had a greater incidence of the disease and for a longer period than School B, also, but very little, to the earlier average age of the boys at the latter school. The difference between the reactions in the younger and older boys is only brought out by differentiating between positive and strongly positive reactions.

School.	Boys Under 14 Years yielding Strong Reactions.	Boys 14 Years and Over yielding Strong Reactions.
A	27%	18%
B	30%	15%

There is a wide variation in the extent of the reaction. The longitudinal and transverse diameters of the erythematous area on the forearm were measured in all cases. The longitudinal diameter varied from over four to less than one centimetre. Some of the boys giving very slight reactions were retested with similar results. The interpretation of these as either reactions or no reactions from the practical point of view is open to criticism. Two boys who failed to yield reactions according to this standard, that is to say, there was only an area of erythema with longest diameter less than one centimetre, developed scarlet fever.

In contrast with this failure of the Dick test others have had more fortunate experiences. For example, the Dicks themselves had under observation 158 nurses who did not give the Dick reaction (not susceptible). These took up scarlet fever nursing for periods of from six weeks to one and a

half years. None contracted scarlatina. A further two hundred and thirty persons who gave no reaction to the test, exposed for shorter periods, failed to contract it. Sixty-nine of these showed the presence of hæmolytic streptococci in nose or throat after their exposure. Four other persons yielding slight Dick reactions, developed sore throat and thereafter there was no response to the test. None of these had a rash, but two desquamated. Such atypical symptoms, they say, are particularly apt to follow exposure to scarlet fever in persons who yield only slight reactions to the skin test or in those who have been incompletely immunized.

#### Active Immunization.

Thirty-two "Dick-reacting" boys from these schools were given three injections of Fairfield toxin, most of them receiving 250, 500 and 1,500 skin test doses, and after varying intervals they returned to school. Two contracted mild scarlet fever within a few weeks. One received the above dosage, the other 125, 500 and 1,500 doses. Neither of them had been tested after immunization. Subsequently another boy was given 250, 500, 1,500 and 3,000 skin test doses, but still reacted to the Dick test three weeks later. However, a further injection of 6,000 was followed by a complete failure to react. There is no doubt that the three doses I set out to give, after some preliminary tests, were insufficient. I desired to avoid severe reactions which might bring the method into disfavour, though I have not been able to find recorded any serious consequences even in large series. Very much better results are quoted abroad. For example, the Dicks immunized 206 reacting nurses until they failed to react. They were then exposed to scarlet fever for periods up to one and a half years, none contracting the disease. Very satisfactory statistical results have also been obtained in Aberdeen.<sup>(23)</sup>

I do not think that any practitioner should be deterred by the failure of immunization in my small series, due no doubt to insufficient dosage. I suggest that severe reactions may possibly be avoided by commencing with 250 doses, then a series of 500, 1,500, 3,000 and 6,000, followed by a Dick test three weeks later. The interval between doses may usually be five days, though sometimes, if the local reaction had not quite subsided, I waited for seven days.

#### Bacteriological Examination of Patients and Contacts.

It has been generally agreed that hæmolytic streptococci may be cultivated from the throat of almost 100% of scarlet fever patients. In the few cases in which I have had an opportunity of examining the throat, hæmolytic streptococci have shown up in large numbers on blood agar plates. I have found that their absence may be of equal value in doubtful cases. The intelligent use of the bacteriological method combined with the Dick and Schultz-Charlton tests may become of value in the diagnosis of doubtful cases, but it seems that a certain amount of practice and experience are required in the use and interpretation of the results obtained.

During convalescence swabbings were made of the nose and throat of a considerable proportion of the patients from these schools. The cultures were made, as far as possible, from the tonsillar crypts or occasionally from any obvious muco-pus on the posterior pharyngeal wall. The nasal cultures were made by the nasal route, a swab stick being passed back to the naso-pharynx. Human blood agar plates were employed and colonies were picked off on to sloped blood agar. The first cultures were made from three to six weeks from the onset of the illness. Of one group of twenty-four boys examined in this way at weekly intervals no hæmolytic streptococci were cultured from seven at the first swabbing, from three at the second, from six at the third, whilst none was cultured from eight only at the fourth, fifth or sixth swabbing or only a very few colonies of hæmolytic streptococci continued to appear until the patients went away. The naso-pharynx was not infrequently found to be infected. Sometimes cultures were obtained from this situation for just as long a period as from the tonsils. In the majority of instances in which cultures showed infection, the tonsils were infected longer than the naso-pharynx, whilst in a minority the converse result was obtained. Swollen or unhealthy-looking tonsils may be expected almost regularly to remain infected longer than tonsils which have settled down. Also wet muco-purulent swabs from the naso-pharynx usually yielded hæmolytic streptococci, though in some cases pneumococci were cultivated in large numbers, sometimes associated with smaller numbers of hæmolytic streptococci. A useful point in the bacteriological identification has been the finding that the somewhat opaque and slightly raised, easily cultivated colonies of the hæmolytic streptococci isolated from patients, convalescents and contacts have usually emulsified readily in water to form smooth films on glass slides. When stained by Gram's method or by Jensen's modification the cocci tend to lose the stain more easily than does the *viridans* type or pneumococci; the hæmolytic cocci are arranged in small groups and occasional short chains, but the definite pleomorphism and agglutinated clumps of the *viridans* type or the oval or lanceolate pairs of the pneumococci are in strong contrast.

A considerable number of school boys who were in a very variable degree contacts of the patients at the onset of their illness, were "swabbed" for hæmolytic streptococci. Of seventy-one previously found to be Dick-reactors six were found to harbour hæmolytic streptococci, the percentage being 8.4. Of twenty-six previously found to be Dick-non-reactors seven harboured hæmolytic streptococci, the percentage being 23. The naso-pharynx was sometimes found infected as well as the tonsils. It had been hoped that carriers, if they might be so called, would be found only amongst the Dick-non-reacting boys. Certainly they were three times as common. It would appear that the hæmolytic streptococci found in the Dick-reacting boys were incapable of

producing scarlet fever in their hosts. I was unable to go into the question of their toxigenic powers or their serological relationships. Taking into consideration all the generally accepted notions as to ætiology, the true carriers should be in the group harbouring hæmolytic streptococci. But do they include carriers of both virulent and avirulent scarlet streptococci or are some carriers of scarlet streptococci and others of other races? This is of the essence of the bacteriological problem. In spite of the Dicks' claims that toxin production is the specific character upon which bacteriological diagnosis should result, and their attack upon the Dochez school of serological classification, it seems very doubtful if the present method of demonstration of toxin production is likely to be of great value in this particular problem seeing that, for example, Eagles<sup>(18)</sup> and the Japanese workers<sup>(25)</sup> have shown that toxin production, though apparently constant in the scarlet strains, is at least not uncommon in the pyogenic, puerperal and erysipelatosus strains and the toxins, whatever their origin, are neutralized by scarlet fever antitoxin. The problem is apparently more complex than diphtheria, in which toxin production is of prime importance in bacteriological diagnosis. There may be in addition factors in the host other than susceptibility to the toxin. It has been suggested somewhere that some local immune mechanism in the throat may prevent an attack of scarlet fever in persons who are shown to be susceptible to the toxin, but who do not contract it after exposure.

In spite of the apparent inaccuracy of the complete statement, as a working hypothesis it might be wise to declare that those convalescents and contacts who harbour hæmolytic streptococci in appreciable numbers, are carriers and potential disseminators of infection. This is going definitely further than Zingher who suggested that failure to demonstrate streptococci on bacteriological examination may be required before convalescents are discharged from quarantine if a method of rapid and accurate bacteriological diagnosis is established. A wide employment of bacteriological methods by public health officers and bacteriologists might throw more light on these problems.

I gratefully express my indebtedness to Dr. Morgan, of the New South Wales Board of Health, to Dr. Morgan, of the Commonwealth Serum Laboratories, and to Dr. S. A. Smith, Dr. Harold Ritchie, Dr. J. Hoets, Dr. E. Ludowici and Dr. F. S. Hansman.

#### Summary.

1. A short statement is given of some of the administrative and bacteriological problems in scarlet fever.

2. Some experiences are related of the use of the Dick test, of active immunization and of bacteriological examination of convalescents and contacts.

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## Reports of Cases.

### CHORION EPITHELIOMA IN A MALE.<sup>1</sup>

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#### CLINICAL NOTES.

(JOHN TANSEY.)

C.P., MALE, aged twenty-five years, was admitted to hospital on May 16, 1928, complaining of pain in the chest, general weakness and loss of weight. The pain commenced two months previously and was situated in the præcordium without any definite lines of radiation.

Fourteen days subsequent to the onset of pain there had been a brisk hæmoptysis of bright red blood. From this time onwards the patient suffered frequent bouts of feverishness and rapidly lost weight. There was a loose, productive cough and the sputum was frequently blood stained, but there was no repetition of the previous frank hæmoptysis. There was no history of night sweats.

There was nothing of importance in the history of his previous health, nor in his family history.

On examination the patient was obviously very ill and had a good deal of respiratory distress. Both breasts were considerably enlarged and both testicles were small, but testicular sensation was retained. There was deficient respiratory expansion of the left side of the chest and a bulging of the anterior chest wall on the left side in the region of the third, fourth and fifth ribs. There was impairment of the percussion note over both sides of the chest, the percussion note over the lower part of the left side of the chest having a flat quality. The breath sounds were distant, mainly bronchial in character and with numerous coarse and fine accompaniments. Examination of the other systems revealed nothing of importance. Apart from the tumefaction of the breasts there was no alteration in any of the secondary sexual characteristics. Some deeply blood stained fluid was removed from the left side of the chest. Cytological and bacteriological examination of this fluid revealed nothing of importance. A searching clinical examination failed to reveal any evidence of a primary neoplasm outside the thoracic cavity.

The patient died twelve days after admission to hospital.

#### DISCUSSION ON POST MORTEM FINDINGS.

(LESLIE UTZ.)

Post mortem examination was conducted at Saint Vincent's Hospital, Sydney, on May 28, 1928.

The external appearances of the cadaver were noted and it was observed that in addition to the emaciated, anæmic and cachetic appearance, both testicles were considerably undersized and both breasts were considerably enlarged. There was no palpable thyroid tumour. The abdominal cavity gave mostly negative results, but the large mesenteric veins were considerably engorged. There was slight congestion of the kidneys and spleen and more pronounced venous congestion of the liver. Pancreas, suprarenals and prostate gland appeared normal. On opening the thorax it was observed that there was a large amount of blood stained fluid on the left side and a small amount present on the right side. The heart and pericardium were considerably displaced to the right.

On the anterior surface of the left lung there was an exudate of old blood clot and fibrin and an obvious tumour of the lung which had caused a definite impression on, but not actual erosion into the overlying ribs.

<sup>1</sup> Read at a meeting of the Medical Sciences Club, Sydney, on July 2, 1928.

The right lung did not present any exudate on its surface, but several large hæmorrhagic tumours were seen on its already exposed anterior surface.

The left lung was difficult to deliver, partly on account of the aforementioned exudate which in a few isolated places had already organized with the result that a few adhesions to the parietal pleura were present and partly because at its extreme apex it was attached to what was considered a substernal prolongation of the thyroid gland (see Figure I).

This fact is mentioned because from the macroscopic appearances a preliminary diagnosis of adeno-carcinoma of a substernal thyroid gland with metastatic involvement of the lungs was made. This diagnosis was strengthened when an ultimate examination of the thyroid gland revealed what appeared to be an hæmorrhagic tumour in its retrosternal prolongation (see Figure II) and it was not until after microscopical sections were examined and the thyroid gland was reexamined that it was discovered that this tumour was not present in the thyroid tissue itself, but was situated in connective tissue and partially surrounded by a substernal prolongation of the thyroid gland (see Figure II).

When the left lung was delivered (Figure III) and examined macroscopically it was found that there was a large spherical hæmorrhagic friable and partially necrotic tumour occupying and replacing the entire upper lobe and the major portion of the lower lobe and separated from the remaining portion of the lower lobe by a more or less indefinite fibrous band.

The remaining portion of the lower lobe contained many smaller hæmorrhagic tumours (not friable) and these were separated from each other and from the larger tumour by more or less normal lung tissue.

The smaller tumours varied in size from spheres of diameter two centimetres to spheres with diameter four centimetres.

The right lung (Figure IV) examined macroscopically revealed the presence of numerous small spherical tumours whose diameters varied from one centimetre to five centimetres. These tumours were similar to those observed at the base of the left lung and were very hæmorrhagic, but not friable. There were no enlarged mediastinal lymph glands present, but there was a small hæmorrhagic nodule on the parietal pleura on the posterior surface of the right thoracic cavity situated over, but not attached to the sixth rib.

Beyond displacement of the heart to the right side, dilatation and engorgement of the right side and the presence of a limited amount of *ante mortem* clot on the right side, there was nothing more of interest observed at the *post mortem* examination.

Histological examinations were made on sections taken from the large tumour of the left lung, several of the smaller tumours and from one of the enlarged breasts. The microscopical appearances of all the tumours were very similar, except that the large tumour contained mainly semiorganized blood clot and it was not so cellular as the smaller tumours. In all tumours lung tissue was practically absent and was almost entirely replaced by hæmorrhages, semiorganized blood clot and by an invasion of large epithelial cells varying somewhat in size and indistinguishable from chorionic cells, both forms, namely syncytial cells and Langhans's cells being observed. The characteristic arrangement was observed: the cells were not grouped into large masses, but were found more or less isolated and wandering in all directions throughout the tissue examined. I wish to repeat that sections from the large tumour contained the smallest number of these cells and it was the large tumour that both macroscopically and microscopically consisted mainly of friable blood clot in varying stages of organization.

The vessels in the tumours were represented by blood spaces and in many cases the chorionic cells were most abundant around these immature vessels.

The microscopical features of these tumours were in all respects identical with those observed in uterine chorionic epithelioma and sections from a case reported by Dr. C. E. D'Arcy in June, 1927, in THE MEDICAL JOURNAL OF AUSTRALIA were selected for comparison (Figure V). (Compare Figures VI, VII and VIII.)

Sections of breast tissue show well marked acini, dilated ducts and some evidence of chronic mastitis.

In reviewing the macroscopical and microscopical findings, I wish first of all to attempt to justify my selection of the term "chorion epithelioma in a male" instead of some of the suggested classifications such as malignant teratoma.

In a recent editorial article styled "Ectopic Chorion Epithelioma," appearing in THE MEDICAL JOURNAL OF AUSTRALIA, June 2, 1928, page 688, the concluding paragraph reads: "At the present time it is wise to conclude that the term ectopic chorion epithelioma should be reserved for those tumours whose relationship to the uterine tissues can be justly inferred and some other name such as malignant teratoma might be used for the others."

In this same article, however, it is stated earlier that: "It is well known that chorionic elements may gain entrance into the maternal circulation. In 1904 Schmorl examined the lungs of one hundred and fifty-eight women who had died at different stages of pregnancy or after delivery. He found chorionic cells in the pulmonary capillaries of 80% of the bodies of those whose pregnancies had been normal."

If, then, chorionic cells are found in the maternal pulmonary capillaries of such a large proportion of cases of normal pregnancies, is it too much to expect that these same cells could occasionally enter the fetal circulation and lodge in the pulmonary capillaries of the fœtus?

If such an entrance into the fetal circulation does exist, is it not possible that these cells could form what may be termed "chorionic rests," which could act as a starting point of malignant disease?

In the same article in THE MEDICAL JOURNAL OF AUSTRALIA an analysis is made of cases in females reported by de Zalka and others and in most of them there appears to be a difficulty in locating a primary tumour and explanations have been advanced, for example, that the primary tumour was either healed or expelled or that the tumour developed from a teratoma which was not discovered. Obviously a teratoma, whether existing in male or female although phylogenetically one generation behind a gravid uterus, can be analogous as regards potential morbid developmental factors.

Therefore it is not difficult to imagine that tumours arising from teratoma would have similar characteristics to those arising from a pathological gravid uterus. But at the same time if no teratoma can be found, one can scarcely attribute the cause to its existence and consequently I advance the hypothesis that just as it is possible for individuals to have twin inclusions such as dermoid cysts and teratoma, so also it should be possible for the individual, at least occasionally, to be the recipient of chorionic cells which have been proved to wander in the maternal circulation as far as the pulmonary capillaries. Surely it is equally possible for tumours to arise from such chorionic rests, if they do exist, just as they do arise from teratoma.

The fact remains that these tumours occurring in males and tumours occurring in females, with or without obvious genital neoplasm, are histologically and morphologically identical and until some other definite conclusion can be advanced, it appears to me to be unwise to draw arbitrary conclusions.

Moreover, I suggest that there could be several analogous features common to an abnormal gravid uterus giving rise to true chorionic cancer and that of a pathological twin remnant or inclusion in an individual male or female and of the latter a typical instance is a teratoma.

Again, in reference to the nomenclature, one cannot overlook the fact that when these tumours are found in males, there are invariably associated certain female characteristics such as have been mentioned in this case.

Hence it seems unnecessary to adopt de Zalka's distinction between these tumours occurring in the different sexes, as set out in the same article in THE MEDICAL JOURNAL OF AUSTRALIA, namely: "De Zalka states . . . that extrauterine chorion epitheliomata may be divided into two classes: those associated with pregnancy and those in which chorion epitheliomatous proliferation occurs in a teratoma."

Before concluding this discussion on aetiology and nomenclature it would be just to mention Bostroem's theory of origin. Bostroem's hypothesis is not accepted by de Zalka and in fact does not find general support. Briefly his hypothesis is that the tumours originate from mesenchymal endothelial cells, the so-called serotinal wandering cells. Quoting from the same article: "Bostroem also thinks that metastases are not products of a primary tumour, but are the result of an irritative action on undifferentiated germ cells in other organs similar to that causing the primary tumour. . . . In this sense metastases are 'sister tumours'."

This theory could at least permit the absence of a primary tumour outside the thorax in our case and it is mentioned because I wish later to suggest that both primary and secondary or "sister tumours" were confined to the thorax.

It is noteworthy that in the majority of cases reported where metastases have been seen, the lungs have not escaped. In fact there would appear to be some selection for the pulmonary tissue and this is an interesting fact and probably not surprising when the results of Schmorl's findings, already mentioned, are considered.

I will now set out some important information to be obtained from reference to a very excellent article by R. M. Handfield-Jones, appearing in the *British Journal of Surgery*, Volume XIII, page 606, entitled: "Chorionic Carcinoma in the Testicle with a Report of a New Case." This article is illustrated by some coloured photographs of metastatic nodules in the lung and some histological microphotographs which are identical in all respects with the corresponding features of our case. The writer points out that Schlagenhauser in 1902 reviewed many previous reports as far back as 1878 and included under the heading of chorionic carcinoma of the testis numerous cases with puzzling histological features grouped under many different headings and Schlagenhauser placed these cases on a firm foundation, attributing their origin to a teratoma.

Handfield-Jones has been very careful not to include in his list of reviewed cases any doubtful ones. He maintains that the following elements are universally found in chorionic carcinoma: (i) The syncytium, consisting of multinuclear masses of varying shape and size and often sending branching processes out into surrounding tissue, (ii) Langhans's cells—medium size polygonal cells with larger nuclei, but less dense cytoplasm than the syncytial cells, (iii) chorionic wandering cells representing a compromise between (i) and (ii), (iv) blood clot and fibrin.

These elements have all been described as being present in our case. Handfield-Jones also states that the lungs invariably are the principal seat of secondary deposits. He gives in detail seven theories of origin of his testicular tumours and he states that "the generally accepted view is that it arises from some element in a teratoma, but that the formation of true foetal membranes is not necessary."

A teratoma without true foetal membranes appears to me to be little more than what I have suggested as a possibility, namely, "chorionic rests."

This article finally concludes with a complete, up-to-date list of 109 cases and a glance at this list is very interesting, for in 30% of these cases no evidence of teratoma was found. Even in his own reported case he states that only a few teratomatous elements were present in the testicle, such as islands of cartilage, some cysts *et cetera*.

Therefore, in reviewing this article it appears to me that some theory of origin is necessary more tangible than the existence of teratoma, half-formed teratoma, some teratomatous elements and sometimes the existence of teratoma that cannot be found at all, such as in 30% of cases reported, and it is the last named group that obviously calls for a more definite theory as regards aetiology.

Finally, I wish to refer to Edmund de Zalka's paper, "Concerning Ectopic Chorionepithelioma" appearing in the *American Journal of Pathology*, January, 1928. In this article we find the additional information that of Schmorl's cases in which he observed the presence of chorionic cells

in the maternal pulmonary capillaries, there was actual chorionic cell proliferation in three. This fact would support the hypothesis that it is possible for malignant disease to develop from these wandering cells.

De Zalka has reviewed the literature of ovarian chorion epithelioma and states that among twenty-five patients there is a history of pregnancy in thirteen, in seven pregnancy is probably excluded and in five the diagnosis is doubtful. De Zalka reviews cases reported by Klotz and Voigt in which no evidence of teratoma could be found. De Zalka's article also includes a discussion on two reported cases of primary chorion epithelioma of the liver. In neither case was there a genital tumour or teratoma found.

In his summary de Zalka states: "In the case of liver chorionepithelioma . . . no teratomatous elements were demonstrable. The case is likewise, therefore, regarded as one of ectopic chorion epithelioma initiated by the transportation in a retrograde manner of chorionic elements through the inferior vena cava."

This explanation may be acceptable for one of his reviewed cases which occurred in a female, but it cannot be the correct theory of origin for the other case which was found in a male aged forty years. De Zalka mentions that in this case in a male no serial sections were carried out to exclude minute teratomatous elements, neither has this course been taken in our case, obviously because the primary tumour is so large that serial sections would be most impracticable. But it must be remembered that in most cases in which the origin of these tumours has been traced to the existence of a teratoma, there have been macroscopical and not minute microscopical elements of teratoma present.

#### Conclusions.

It is suggested that in this case there is a primary chorion epithelioma present in the left lung which tumour occupies the greater portion of that organ. It is very friable and is separated from the remaining lung tissue by an indefinite fibrous band.

There are secondary nodules present in both lungs and elsewhere. The suggested origin of these tumours is that the primary tumour has developed from "chorionic rests" and chorionic cells gained entrance through the foetal circulation (*in utero*), just as chorionic cells have been proved to enter the maternal circulation during pregnancy and lodge in pulmonary capillaries of the mother.

#### Acknowledgement.

I wish especially to thank Dr. Keith Inglis who gave me very valuable assistance in the original diagnosis, Dr. A. J. Fitzgerald for suggestions as regards aetiology, and Dr. E. M. Humphrey for microscopical photographs.

#### TREATMENT OF CANCER OF THE LIP BY RADIUM NEEDLES.<sup>1</sup>

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For the information of those gentlemen present this evening whose duty it will be in the near future to treat patients suffering from cancer by means of radium needles, I have endeavoured by demonstrating the following two cases to illustrate the method of inserting and retaining the needles in position. I would point out that, even in cancer of the lip, good local results may be obtained, especially in those cases in which treatment by the knife would mean big mutilating operations.

CASE I.—The first case is that of a man, J.W.M., aged thirty-five years, teamster. He was first seen by me on September 12, 1928, when he gave a history of "growth on the lower lip for over twelve months" (see Figure I).

<sup>1</sup> Read at a meeting of the Surgical Section of the Queensland Branch of the British Medical Association on November 23, 1928.

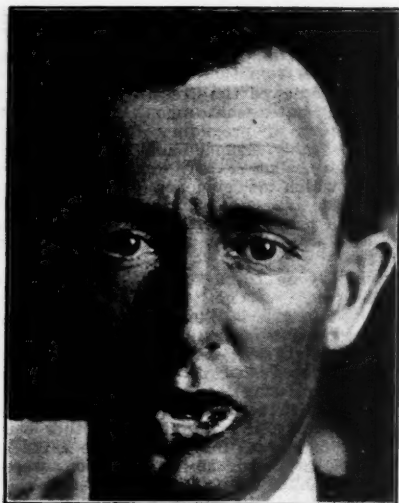


FIGURE I.

Patient in Case I with recurrent epithelioma of lip on September 13, 1928.

Twice it had been removed surgically, the last operation being performed six months previous to the above date. For the last five months he had been under a "quack," who had been "burning it with arsenic." There is no history of syphilis. The condition was that of a large, typical epithelioma of the lower lip to the left of the mid-line and involving most of the lip on that side. This growth was continuous with an ulcer which spread around on to the buccal aspect of the scar tissue on the right half of the lip. Submentally, a hard "orange seed" gland was palpable. It was not fixed. The Wassermann test performed by Dr. Avery yielded no reaction. On September 14 nine 1 milligramme and four 0.5 milligramme radium needles were inserted under local analgesia into the lower lip. The needles used contain 0.5 and 1.00 milligrammes of radium and are of platinum of 0.5 millimetre screening. They are spaced approximately two centimetres apart and are left in position from four to seven days or longer. Figure II shows the needles *in situ*. This illustrates Douglas Harmer's method of retaining the needles

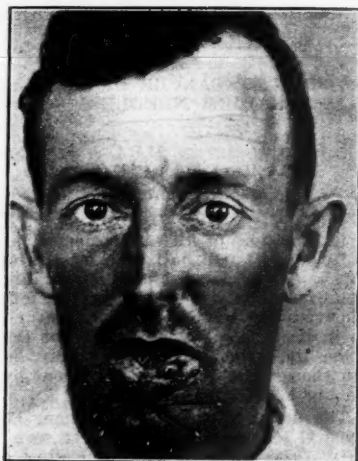


FIGURE II.

The same patient, showing nine 1 milligramme and four 0.5 milligramme needles, after being in position for four and a half days. There is already evidence of reaction, September 18, 1928.

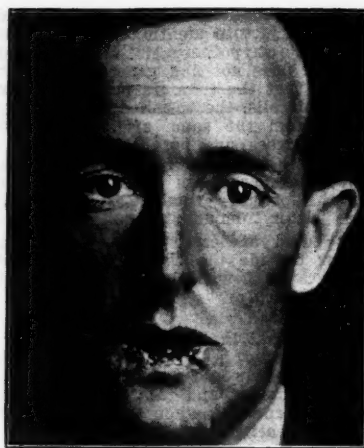


FIGURE III.

The same patient, twenty-one days after insertion of needles, 1,308 milligramme hours radiation, October 5, 1928.

in position. It was described by me in THE MEDICAL JOURNAL OF AUSTRALIA of November 24, 1928. A section was taken at the time and this was reported upon by Professor Welsh, of the University of Sydney, as "a definite squamous epithelioma, with typical cell nests." The radium needles were removed in two stages, the total amount of exposure being 1,308 milligramme hours. The patient was kept in hospital for one week. Subsequently, he had a pronounced reaction in the chin area and there was a little ulceration of the mucous membrane of the lip and a certain degree of gingivitis with definite pyorrhea. The submaxillary lymphatic gland on the right side enlarged quite considerably, but it has since gradually subsided, until it is now the size of a hazel nut. I do not think that this is more than an inflammatory enlargement of the gland. However, the patient is undergoing gland dissection within a few days. The photographs (Figures III and IV) show the stages in the recent history of the case. It will be noticed that there is now no sign whatsoever of any ulceration and that the tissues in the neighbourhood are distinctly soft and pliable.

CASE II.—Case II is of a man, W.H.G., aged fifty-one years, a farmer. He gives a history of "always having had a skin which was very susceptible to sunburn." For six years or more he was subject to "scale on the face" in

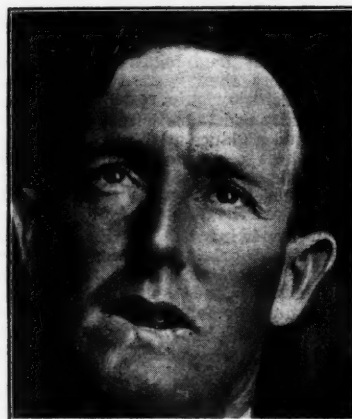


FIGURE IV.

The same patient, eight and a half weeks after insertion of radium needles, November 12, 1928.



FIGURE V.

Case II, man, aged fifty-one, with recurrent rodent ulcer (transitional) showing 11 one-milligramme needles after two days in position, September 19, 1928.

several places. In July, 1924, he had an operation on the right cheek, when a "small cyst" was removed. There then appeared an ulceration which was treated by X rays. He was next operated upon in April, 1925, and later had X ray treatment under Dr. Val. McDowall. I understand from Dr. McDowall that he was advised on several occasions to return for further surgical treatment, but that he objected to doing this. When I saw him on September 14, 1928, he presented a large ulceration of the right side of the face which was attached to the lower border of the malar bone and to the outer wall of the superior maxilla (see Figure V). The masseter muscle was considerably involved and there was much induration over the mandible. There was definite ulceration of the inside of the cheek and no opening movement was possible at the right temporo-mandibular joint. Eleven one milligramme needles were inserted into and around the growth under general anaesthesia. A specimen of the growth was removed and was sent to Professor Welsh of the University of Sydney who reported as follows:

The growth is one of those basal-celled epitheliomas which is half-way between a true rodent and an ordinary, squamous epithelioma; therefore, more malignant than the former and not quite so malignant as the latter.



FIGURE VI.

The same patient, ten weeks after insertion of radium needles, 1,870 milligramme hours, November 23, 1928.

All the needles were removed after an exposure of 1,870 milligramme hours. The photographs (Figures V and VI) show stages in the progress of the case. It will be seen that the growth has practically healed and that the tissues in the immediate neighbourhood are soft and pliable. It is proposed to watch this patient carefully with the object of excising at a later stage the fibrous tissue which has taken the place of the masseter muscle, in order to allow movement at the temporo-mandibular joint. The area uncovered by epithelium is gradually reducing daily.

#### Acknowledgement.

I wish to thank Dr. Donald Cameron and Dr. Val. McDowall for referring these patients to me for treatment.

#### A CASE OF EPISTAXIS WITH UNUSUAL SEQUELÆ.

By ASHLEIGH O. DAVY, M.B., Ch.M., D.L.O.,

Honorary Assistant Ear, Nose and Throat Surgeon,  
Royal Prince Alfred Hospital and Royal  
Alexandra Hospital for Children,  
Camperdown.

R.C., a male, *ætatis* thirty-four years, was admitted to the Royal Prince Alfred Hospital on September 14, 1928, with a history of severe epistaxis of spontaneous origin off and on for four days. His nose had been packed on the preceding day and again at his home that morning, but the bleeding was not controlled.

On admission the House Surgeon inserted two post-nasal plugs and packed the nose again under general anaesthesia. This controlled the bleeding.

On the fifteenth the plugs and gauze were removed and the bleeding did not recur.

On the seventeenth the patient complained of earache in both ears and "slight redness of the left drum" is reported to have been present. The evening temperature was 38.8° C. (102° F.).

On the eighteenth the writer saw the patient for the first time. Severe earache was present in both ears. There was slight tenderness over both mastoid processes. His temperature was 38.6° C. (101.6° F.). Both drums bulged and were yellow. Double paracentesis was performed under general anaesthesia and profuse purulent discharge was obtained from both sides.

On the nineteenth the earache was relieved and both ears were discharging profusely.

On the twentieth there was again pain in both ears. The temperature was in the region of 38.8° C. A profuse discharge was still present. The patient appeared somewhat cyanosed. A patch of dulness with bronchial breathing was present below the left clavicle and there was impaired resonance with crepitations at both bases.

On the twenty-first there was definite double mastoiditis with considerable pain and tenderness over both mastoid processes. His temperature was 38.8° C. (102° F.) and his respirations were thirty-two per minute. His general condition was poor. He was cyanosed. The chest signs were unchanged. He was seen by the Honorary Physician (Dr. Cosh) in order that he might advise whether or not the patient would stand a double mastoid operation under general anaesthesia. He reported: "I regard him as a very bad subject for anaesthesia, he is dusky about the lips and the heart sounds are soft and faint; if the operation is imperative to save his life, he might take his chances as regards the anæsthetic."

I therefore decided to attempt to drain his mastoids under local anaesthesia. Morphine hydrochloride 0.01 gramme (one-sixth of a grain) with atropine sulphate 0.0006 gramme (one-hundredth of a grain) was administered hypodermically half an hour before the operation. A 2% "Novocain" solution with two mls of adrenalin in each hundred mls was injected subcutaneously round the operative field on the left side and down along the posterior wall of the meatus. With the assistance of Dr. M. R. Flynn the

second and third cervical nerves were blocked by deep injection behind the sterno-mastoid.

The incision was made down to the bone and a further injection of "Novocain" given under the periosteum. The mastoid was large and very cellular and pus was found in all the cells including the tip, which was taken away, and in the root of the zygoma. The wound was packed and left open.

The patient stated that he had experienced little pain or discomfort and it was decided to proceed immediately with the opposite side.

A slightly different method of anaesthesia was used. Cervical block was again employed and the posterior meatal wall again injected. The auricular-temporal nerve was then injected; no injections were used to surround the field of operation.

Anaesthesia was equally satisfactorily and more rapidly obtained, but after the incision a subperiosteal injection was again necessary. Extensive suppuration of this mastoid was also found and it was again necessary to take away the tip and to follow the cells into the root of the zygoma.

The whole procedure took two hours and disturbed the patient very little.

From then on the patient went along satisfactorily, his chest condition settled down and he eventually made a complete recovery.

#### Comment.

The patient was a fat unhealthy man, with a very strong alcoholic history and probably small powers of resistance.

The aural infection was undoubtedly secondary to the repeated (although unavoidable) packing of the nose and the post-nasal plugging.

The most sensitive part in the field of operation was the portion of the posterior meatal wall supplied by the auricular branch of the vagus.

Chiselling the cortex of the mastoid was only slightly felt and chiselling or manipulations in the mastoid cells, which are supplied by the tympanic branch of the glossopharyngeal nerve through the tympanic plexus, was quite painless.

No attempt was made to inject the tympanic plexus with "Novocain" and not even a topical application of cocaine to the cells was required.

Altogether eighty-five cubic centimetres (three ounces) of 2% "Novocain" solution with a total of 1.8 cubic centimetres (thirty minims) of adrenalin were used.

Considerably less bleeding was met with during the operation than is usual when general anaesthesia is employed.

## Reviews.

### OSLER'S MEDICINE.

THE issue of a sixth volume entitled "Diseases of the Nervous System, Diseases and Abnormalities of the Mind," completes the revision of Osler's Modern Medicine.<sup>1</sup> The fact that it has been found possible to record our knowledge of modern medicine in 1928 in one volume less than was needed in 1927 is an evidence of the determination of the contributors to eliminate all superfluous matter, but we have thought at times that this effort at brevity has led to the exclusion of useful material.

The "Introduction to Diseases of the Nervous System," by Llewellyn F. Burke, which fills the first eighty pages, sets a high standard that is on the whole well maintained.

Harvey Cushing has considerably embellished his article on intracranial tumours which was probably the one most frequently consulted in the previous edition, while the delightful essay on diseases of the cerebral blood vessels, by the late Henry M. Thomas, has been almost untouched

by his son, Henry M. Thomas, junior, to whom the revision has been entrusted.

The least satisfactory article in the whole volume to our mind is that on epilepsy, by D. T. Pierce Clarke, which replaces the very sane and readable account of our then knowledge of the subject by William P. Sprattling in the 1910 edition. It was to be expected that the psycho-analytical aspects of this disease would in these times receive full consideration, but we feel that Dr. Clarke has overdeveloped the thesis. Those who have not closely followed the work of Freud and his school, will find themselves involved in an entirely new train of thought when they read that "the epileptic reaction from its mildest to its severest reaction is a protection, for it obliterates reality and reduces the subject to the lowest level of organic response—that of a comatose state. Hence the fit is really a protective mechanism . . . . It dispels an intolerable demand and the epileptic retreats to a state of harmony and peace." He would well need to seek such peace, for Dr. Clarke tells us: "At heart the epileptic is the most pitiable of oral and anal erotics."

Having found what a weird personality his patient is, the reader will turn to the section of treatment with a sinking feeling that he has been all astray in his therapeutics and he will find his fears are well grounded. "Bromides and sedatives lower the epileptic's resistance to difficult adaptations; his whole responses are made more difficult." Dr. Clarke states that he himself employs bromides for less than 5% of his patients.

His statement that in handling the individual epileptic it is first necessary to analyse the specific conflicts which he has to meet in life and note his type of mismanagement of them, is followed by something more than a page of what we believe would be regarded by more than 50% of those who turn to this article for guidance, as incomprehensible jargon. Those few who do succeed in understanding the principles of treatment inculcated, will find a difficulty in applying them when confronted with a child of under three years of age, the stage at which the ordinary practitioner is most often called upon to treat the disease. The example provided of a suitable diet card is as clear and dogmatic as one could wish, but the rationale is quite unintelligible. After reading that as a general rule the more or less complete exclusion of meats will be found advantageous, we find that for both luncheon and dinner the patient is allowed a choice of fresh fish, chicken, lamb and mutton. Steak and roast beef are sternly forbidden, no doubt as too stimulating to the erotic tendencies and this has at least the backing of hoary tradition, while the lamentable affair in the Garden of Eden may explain the denial of raw apples, but why are oranges and grape fruit on the proscribed list?

Dr. Smith Ely Julliffe has largely rewritten his excellent article on hysteria and of special interest is his full account of the modern views as to the explanation of the peculiar characteristics of this extraordinary reaction.

It seems hypercritical to look for faults in such a readable article as that by B. Sachs on syphilitic diseases of the central nervous system, yet the absence of the abdominal reflexes is so constant a feature in multiple sclerosis that it is surprising to find it stated that such absence in multiple cerebro-spinal syphilis is one of the chief points on which to rely in distinguishing between the two diseases.

Here and there one meets with statements that will hardly find general acceptance, as for example, in the account of combined system diseases of the spinal cord by William G. Spiller, where he states: "The blood changes found in these cases are more of the nature of a secondary anaemia than the pernicious variety." Again, despite the statistical data which he supplies, their clinical experience will prevent most readers from agreeing with Dr. Daniel McCarthy's view that "the evidence is far from conclusive as establishing a distinct causal relationship between rheumatic fever and chorea."

The volume concludes with a short article on the diseases and abnormalities of the mind by Edward A. Strecker. It is a fitting ending to an admirable work and would be very profitable reading for the whole profession, serving to bring home to all the paramount importance of keeping a watchful eye upon the psychic aspect of every patient.

<sup>1</sup> "Modern Medicine, its Theory and Practice," Edited by Sir William Osler, Bart, M.D., F.R.S., Re-edited by Thomas McCrae, M.D., Assisted by Elmer H. Funk, M.D.; Volume VI.: Diseases of the Nervous System; 1928. Philadelphia: Lea and Febiger; Sydney: Angus and Robertson, Limited. Royal 8vo., pp. 964, with illustrations. Price: 42s. net.

## The Medical Journal of Australia

SATURDAY, MARCH 30, 1929.

### The Control of Poliomyelitis.

IN the year 1925 the municipal health officers of the metropolitan district of Melbourne prevailed on the City Council to establish a special committee for poliomyelitis. Convalescents from the disease and those who had had it in the recent past were sought in order that the committee might hold supplies of immune serum. The Director of the Commonwealth Serum Laboratories and his staff and the Director of the Walter and Eliza Hall Institute and his staff lent their aid in the preparation and storage of the serum for therapeutic purposes. An appeal was made to the medical profession throughout the State of Victoria to cooperate with the committee in its campaign to eradicate poliomyelitis. Dr. Jean Macnamara acted as consulting medical officer and aided by her colleagues planned a very efficient attack. The committee has continued its operations each year, but is still faced with a very difficult problem. It is quite obvious that much harm may be done if the attention of the public is directed to the occurrence of this disease. Such a step would certainly give rise to a scare, notwithstanding the fact that the incidence of the disease does not warrant any alarm. The number of infections notified during the year 1928 in Victoria is 186. There were twenty-seven deaths; this is equivalent to a case mortality of approximately 14.5%. The disease was more prevalent between January and April than during the remaining months of the year. The greatest number of notifications was received in February. Up to the present date the incidence does not appear to be lower this year. It is of importance to note that the mortality reached its height among children between the ages of six and sixteen years. Two adult patients, aged fifty-five and forty-four respectively, died. It must be admitted that a disease that claims one victim among each ten thousand of the population and that leads to the death of one person in each seventy-four

thousand, is not a grave menace to the public health when compared with diseases like tuberculosis, syphilis and carcinoma. But preventive medicine demands that every disease that can be controlled, should be attacked vigorously at its source. Moreover, the effects of poliomyelitis on the individual are so serious that if the paralysis can be prevented by prompt and scientific treatment, no effort or expense should be spared to achieve this end.

In her report on the work of the committee during the year 1928, Dr. Jean Macnamara states that six hundred cubic centimetres of serum are held in cold storage in various centres throughout the country districts, while over one litre is available in Melbourne. About a hundred cubic centimetres are required for the treatment of one patient. The experience gained since the institution of the committee justifies the conclusion that if immune serum be given in the preparalytic stage, complete restitution to health usually follows. Dr. Macnamara is prepared to give assistance to any medical practitioner who may be in doubt concerning the diagnosis or who is not familiar with the correct procedure in regard to treatment. We would urge every medical practitioner to read and reread the articles published in our issue of September 1, 1928. This will remind the general practitioner to think of poliomyelitis whenever he encounters a febrile condition in a child that is not typically scarlatina, morbilli, enteric fever, tuberculosis or dysentery. To miss the diagnosis until the signs of paralysis appear means to deprive the patient of his best chance of escaping the disabling results of this disease. Dr. Macnamara has reported that twelve of the patients in Victoria who had the disease in a severe form before they were placed under treatment last year, will probably be dependent on others during the rest of their lives and that a further fifty will be handicapped by permanent paralysis to a greater or lesser degree. Work is being carried out by Dr. F. M. Burnet of the Walter and Eliza Hall Institute and Dr. Macnamara for the purpose of determining the amount of deterioration of immune serum after storage for varying periods. In the meantime use should be made of the available serum in all parts of the State. It

should be recognized that while treatment at an early stage is in itself not a prophylactic measure, the result of early diagnosis and control will certainly be to limit if not to prevent the spread of the disease from the patient. The committee is aiming at a complete suppression of poliomyelitis in Victoria. This objective cannot be achieved unless every practitioner in the State is on the watch and places every child who might have poliomyelitis, under control before paralysis has had time to make its appearance. The committee will lend its aid in discovering the source of infection and in rendering the person spreading the infection harmless to the community by isolation.

### Current Comment.

#### STREPTOCOCCAL PUERPERAL INFECTION.

IN her important contribution to this journal in July of last year on the bacterial flora of the female genital passages Lucy M. Bryce drew several noteworthy conclusions. In the first place she showed that in fever following childbirth or abortion the presence of organisms in the genital tract and especially in the uterus, is often associated with a mild type of disease. She showed that the type of organism discovered was of importance. The presence of a hardy saprophyte indicated to her that the resistance of the host is sufficient to inhibit the growth of harmful parasites. On the other hand the presence in pure culture of such an organism as *Streptococcus pyogenes* appeared to indicate the accession of invasive power which was associated with virulence for the host. Bryce's work also indicated that the presence in the genital passages of streptococci did not necessarily mean that they were causally related to any disease which might exist. It was thought that many of the streptococci found *post partum* are members of the saprophytic flora which temporarily invades the normal puerperal uterus. Bryce's work may well be considered in conjunction with a report recently published by John W. Harris and J. Howard Brown.<sup>1</sup>

These observers have made a clinical and bacteriological study of one hundred and thirteen puerperal infections due to streptococci. It is the routine custom at the Johns Hopkins Hospital to make bacteriological studies of the lochia in all patients who manifest rises in temperature to 38.3° C. (101° F.) or higher on two successive days during the first ten days of the puerperium as well as of all patients with incomplete abortion and *intra partum* infection requiring operative intervention.

It is not necessary to give details of the method used for the collection of lochia; it must suffice to

state that precautions were adopted to secure specimens that were uncontaminated. In a period of a little over twelve months samples of lochia were taken from one hundred and sixty-eight patients. From one hundred and thirteen streptococci were obtained either in pure culture or in association with other organisms; in nineteen instances streptococci were grown in pure culture. Details are given of eleven cases of incomplete abortion. In seven instances the predominant bacteria were aerobic,  $\beta$ -haemolytic streptococci; in two they were aerobic, non-haemolytic streptococci and in the remaining two instances the infecting organisms were anaerobic streptococci, one of which was of the  $\beta$ -haemolytic variety. Ten of the eleven patients recovered and in only one instance did the infection extend beyond the uterus. The labour of twenty-eight of the one hundred and thirteen patients was terminated by an operative procedure. In eleven instances the operation was the low application of forceps. The infection of two patients extended beyond the uterus and in both of these the low forceps operation had been performed. Two patients died. One of these suffered from *placenta praevia*, the operation consisted of the insertion of a bag and the streptococci discovered were of the anaerobic, non-haemolytic type. The other patient who died, suffered from eclampsia, the cervix was manually dilated and craniotomy was performed; the streptococci found were of the aerobic,  $\alpha$ -viridans type and the other organisms isolated included *Bacillus welchii* and *Bacillus coli communis*. In the other patients the fever lasted from three to seventy-three days and the end result in all is described as excellent. In eighteen instances the streptococci were of the aerobic and in ten of the anaerobic type. Seventy-four patients were delivered spontaneously at term. These have been divided into three groups: those who presented various complications during labour or the puerperium, those without complications, in whom rupture of the membranes occurred, vaginal examinations were made or perineal lacerations were sustained, those in whom none of these complicating factors was present. Aerobic streptococci of the  $\beta$ -haemolytic variety were isolated from three patients of the first group, from six patients of the second group and from one patient of the third group.

The first conclusion drawn by Harris and Brown is that puerperal infection due to aerobic,  $\beta$ -haemolytic streptococci is exogenous in origin. They are presuming that whenever streptococci are found in the uterus in the puerperium, these organisms are the cause of the patient's illness. While it is highly probable that in the majority of instances this is the case, sufficient information as to the patient's condition is not given to allow this determination to be made. It would be necessary in all cases, especially in those in which the pyrexia was not of long duration, to exclude breast conditions and other possible causes. Bryce has shown that streptococci may be recovered from the uterus when the puerperium is afebrile. Further, while it would appear that the finding of microorganisms

<sup>1</sup> Bulletin of the Johns Hopkins Hospital, January, 1929.

during the puerperium, identical with those found before labour started, is essential for the formation of definite conclusions, it must be remembered that Bryce has shown that, while the conditions of cervical flora during the first stage of labour resemble that found during pregnancy, a complete change takes place during the puerperium. Even in cases in which vaginal bacilli alone or associated only with staphylococci were present *ante partum*, in the puerperium streptococci (occasionally hæmolytic), staphylococci, diphtheroids and coliform organisms were frequently present in both cervix and uterus. This is not difficult to understand, for the interior of the uterus would provide a much better culture medium after delivery than before. Harris and Brown attach great importance to the fact that aerobic  $\beta$ -hæmolytic streptococci were found in only one of the twenty-five patients delivered spontaneously without any previous manual or operative interference. They conclude that infection is due to this type of organism in most instances introduced from outside at the time of the labour or during the puerperium. They hold, moreover, that there is sufficient evidence to show that the  $\gamma$  non-hæmolytic streptococci are frequently harboured in the vagina and cervix of normal, pregnant, parturient women. They point out that if these streptococci occur in this situation, it is probable that their upward extension into the uterus must sometimes occur at the time of labour. It may be granted that streptococci reach the uterus in this way, but these observers write as if the extension of the microorganisms into the uterus were the only additional factor. There is a grave danger in discussions of this nature, on the presence of microorganisms of various sorts, to lose sight of the part played by the resistance of the patient.

Harris and Brown are perfectly correct in drawing attention to the necessity for the limitation of unnecessary vaginal examination and operative interference at the time of labour. The term "meddlesome midwifery" has come to stay; but this is not the end of the matter. Obstetricians must not lose sight of the necessity for the care of the woman's general health during the months of pregnancy. Her general condition and her bodily tone demand such attention that when labour supervenes her natural resistance will be sufficient to overcome the onslaught of streptococci which may either be introduced from outside or, being already "in residence," are prepared to take advantage of a suitable nidus to extend their activities.

#### PERNICIOUS ANÆMIA AND SPRUE.

THE close resemblance between pernicious anæmia and sprue has been the subject of numerous discussions. The symptoms and the blood picture may bear a striking resemblance. There are generally, however, definite points in which the two diseases differ. For example, the typical frothy "sprue stool" is not seen in pernicious anæmia nor is free hydrochloric acid found in the stomach in pernicious

anæmia. At the same time it has been pointed out by some observers that it may be impossible to distinguish the two conditions. The recent work on pernicious anæmia is well known. A discussion on the pathogenesis of pernicious anæmia in the light of results obtained by liver feeding will be found in THE MEDICAL JOURNAL OF AUSTRALIA of June 30, 1928. The causation of sprue has not been definitely determined. For a long time it appeared as if Ashford had settled the question by the isolation of the *Monilia psilosis*. Reference to this question will be found in these pages in the issues of March 21, 1925, and May 12, 1923. *Monilia psilosis* was also found in the fæces of patients with pernicious anæmia. It is now generally conceded that the *Monilia psilosis* is a secondary factor in both conditions. Good reasons for this view as far as sprue is concerned have been advanced by Hamilton Fairley and Mackie. These observers reached a conclusion which, if it be accepted, allies sprue very closely with pernicious anæmia. Their words may well be quoted. They regard sprue "as due to some infective agency primarily involving the mucosa of the alimentary tract and leading to the generation of toxic substances which deleteriously affect the blood elements, bone marrow and parenchyme cells of the internal organs." It will be seen at once that this definition might almost be applied to pernicious anæmia. The results of liver feeding have had a great deal to do with the formation of the present conception of the causation of pernicious anæmia. It is therefore of interest to read a recent report by Arthur I. Bloomfield and Harry A. Wykoff.<sup>1</sup> They have adopted liver feeding for two patients who were suffering from sprue, and have obtained satisfactory results. They point out that, while liver is mentioned occasionally in the literature as being beneficial, they can find no accounts of adequate liver feeding in sprue in the sense in which it has been carried out in pernicious anæmia. The first patient was a man, aged twenty-five years, whose symptoms and signs were those of sprue. The blood count was that usually found in sprue. Examination of the gastric secretion revealed the presence of free hydrochloric acid. The authors lay stress on this observation (it was made in the second patient) in the differential diagnosis from pernicious anæmia. Liver extract, equivalent to four to six hundred grammes of liver substance, was given and in five weeks the patient was free from symptoms. The second patient was a man, aged fifty-seven years. His clinical history was similar to that of the first patient. The liver extract was given at intervals of a few days and in larger quantities than those given to the other patient. In less than five weeks the patient was apparently well. It must be pointed out that the period of observation of these two patients after their treatment was not sufficiently long to justify any opinion as to the ultimate result of the treatment. The report must be regarded as pointing the way for further work in the treatment of sprue.

<sup>1</sup>The American Journal of the Medical Sciences, February, 1929.

## Abstracts from Current Medical Literature.

### MEDICINE.

#### Ulcerative Colitis.

At a discussion before the Harveian Society on the treatment of ulcerative colitis (*The Lancet*, April 28, 1928) H. L. Tidy stated that ulcerative colitis might be acute or chronic. Many infections lasted for years and the condition was often fatal. Warmth was most important, even in tropical climates; the extremities should be wrapped in wool. Fluids should be given in small quantities, 30 or 60 cubic centimetres (one or two ounces) every twenty minutes in acute cases during waking hours, with a total of two or two and a half litres in twenty-four hours. Vaccines are of little use and serum only in the early stage of bacillary dysentery. Aromatic sulphuric acid and charcoal are sometimes useful given by the mouth. Morphine should never be administered. Starch, thirty or forty-five grammes (two to three ounces), and tincture of opium, two to eight cubic centimetres (half to two fluid drachms), should be administered by the rectum at nights to insure rest, for not more than five days a week and never for more than three days in succession. Irritation of the rectum is to be avoided by these intermissions in treatment. If after three weeks the number of stools per day has been halved, colonic lavage with normal saline or sodium bicarbonate solution, fourteen grammes to a litre (two drachms to a pint), should be commenced. The pressure should be thirty to forty-five centimetres (twelve to eighteen inches) and half an hour should be taken in the administration, the patient lying on alternate sides while the fluid is being injected; the fluid reaches the caecum in this way. Three lavages a week and not on more than two successive days should be given. If the number of stools increases a return should be made to the starch and opium enema for a time. After six or eight months of this treatment medicated enemata may be tried, two cubic centimetres (half a drachm) of "Albargin" to nine hundred cubic centimetres (thirty ounces) of water introduced one hour after colonic lavage. A maximum of six enemata per fortnight should be given, followed by a week's rest. These medicated enemata tend to irritate the colon and for that reason should not be used too soon nor too frequently. L. Norbury stated that hydrochloric acid given by mouth is a benefit to those patients in whom achlorhydria is found. He advised a liberal diet including vitamins, fats and fruits. He suggested many remedies by mouth and holds that blood transfusion is useful in some cases. If the patient does not respond to ordinary medical treatment, appendicostomy is advised, with lavage

through the appendix. Several years are necessary for cure by this means. B. Smith suggested adding adrenalin to the opium enema. C. P. G. Wakeley advised caecostomy or right colostomy if the ulcers are deep. Sigmoidoscopic examination will reveal this. It was generally agreed that the aetiology is uncertain and that relapses are almost inevitable.

#### Diphtheria Immunization.

G. FRANKL, H. HERZIG AND E. NOBEL (*Wiener Medizinische Wochenschrift*, September 8, 1928) comment on the world-wide concern regarding the risks following immunization against diphtheria with toxin-antitoxin. They give a detailed description of their results with anatoxin. In all 163 children were treated. Most of them reacted to tuberculin, but none was in an active stage. The first dose given was 0.5 cubic centimetre followed by one cubic centimetre after an interval of three weeks. A third dose, as recommended by Ramon, was not given. Six weeks after the commencement of immunization 93.8% failed to react to the Schick test and at eight weeks the percentage was 100. Fifty-seven were observed for longer periods and in 14% of these the immunity did not last for more than six months after the second injection, possibly a third dose would have prevented this. In the whole series thirteen contracted diphtheria, five of these were noted within three weeks of the first injection when the effect could hardly have been expected to have taken place. In the remainder three children who developed diphtheria on the fiftieth and fifty-first days, had given no reaction to the Schick test for six weeks. A severe local reaction was present in 1.5% of the children after the first injection and in 17% after the second. The infiltration reached its maximum on the second or third day and then rapidly subsided, leaving a slight pigmentation. In two cases there was some inguinal adenitis. In eight cases after the primary injection and in twenty-four after the second a severe general reaction was noted. The continued fever up to 39.7° C., apathy and headache caused grave concern in spite of a good pulse. The authors conclude that unless the practitioner is prepared to supervise his patients carefully, this method of immunization is not yet advisable for general use.

#### Phosgene Gas Poisoning.

C. HEGLER (*Deutsche Medizinische Wochenschrift*, September 14, 1928) describes the effect of phosgene gas on the inhabitants of a Hamburg suburb when a tank of the gas leaked during the summer of 1928. Seven deaths occurred among 195 patients admitted to his hospital. The first symptoms noted were pain in the chest, cough, bad taste in the mouth and occasionally vomiting. Epigastric pain lasted for a considerable time with most of the patients. There was

increased secretion not only of the lachrymal glands, but also of the bronchial tract. The characteristic odour of phosphorus was noted in the breath of all the patients. There was an apparent incubation period of three to four hours during which the patients felt well. Pulmonary oedema occurred within two hours and in several instances owing to its severity death soon ensued. Dark skinned persons were less affected than fair ones who presented a reddened and cyanotic appearance. Difficulty in respiration and the secretion of a sticky blood-stained sputum were common. The general picture at this stage was that of severe respiratory disturbance associated with full consciousness. In the patients surviving the pulmonary oedema, signs of circulatory failure occurred. The blood was considerably thickened and the haemoglobin index rose to over 100%. Following on venesection the blood flowed very slowly and was of a chocolate colour. The amount of haematin in the blood serum did not run parallel with the severity of the disease in many instances. All severe cases were characterized by a pronounced fall in blood pressure associated with tachycardia, while during convalescence bradycardia was present in most instances. The temperature was not raised, no oedema occurred except in the lungs and ocular changes were also missing. The convalescence was noted for the amount of chronic bronchitis present, although bronchopneumonia and bronchiectasis did not occur. No urinary changes were observed; neither did acute yellow atrophy of the liver nor nervous lesions develop. As regards treatment the author found that venesection with removal of five hundred to eight hundred cubic centimetres of blood and intravenous doses of calcium were useful. No success followed the use of intravenous injections of glucose nor of "Lobelin." The patients felt relieved after oxygen inhalations. Intravenous injections of strophanthin were invaluable for all with severe symptoms. Full details of the autopsy examinations as well as the biochemical investigations of the blood are given.

#### Gastric Changes in Chronic Lead Poisoning.

K. GUTZET (*Münchener Medizinische Wochenschrift*, September 21, 1928) states that, while the cardinal symptoms of acute lead poisoning are well known, in the chronic type they are more subjective in character and related to the alimentary tract besides being not in keeping with the results of physical examination. Little help is obtained from examination of the gums, cutaneous changes and the basophilic stippling of the red corpuscles, for these are often absent. Anæmia is not of a severe type and equal grades are seen in other workers in closed rooms. Spasm is often not seen on radiological examination and there remains a history of dyspeptic symp-

toms, abdominal colic and some nervous symptoms. Gastric analysis was performed in fifteen instances with the following results: Hyperacidity in eight, no free acid in three, decrease in acidity in two and in two the findings were normal. Endoscopic examination of the gastric mucosa revealed hypertrophic changes in nine instances, superficial catarrh in two and atrophic changes in two. True peptic ulcer was observed in only four patients. Lead can reach the stomach directly by ingestion or indirectly through the blood stream after absorption in the lungs. From his animal experiments the author considers that the gastric changes are due more to lead circulating in the blood than to a direct action on the mucosa. Chronic dyspepsia in any person connected with lead while at work must always raise suspicion of lead poisoning and this can be confirmed by analysis of the stomach contents and by direct inspection of the mucosa.

#### Treatment of Laryngeal Tuberculosis.

K. WESSELY (*Wiener Medizinische Wochenschrift*, September 29, 1928) states that laryngeal tuberculosis is practically always secondary to a pulmonary infection. It occurs in 10% of early cases of pulmonary tuberculosis and in at least 50% of the more advanced infections. Infiltration of the mucous membrane is first seen followed by loss of epithelium in places and finally definite ulceration. Oedema of the surrounding tissues is always present and miliary tubercles may also be seen. In contradistinction to tuberculosis elsewhere in the body pain occurs early and is severe. Dysphagia of varying degree is noted and in severe cases the unfortunate patient is afraid to eat or drink. Local treatment of the larynx must be combined with general constitutional remedies, especially rest in bed. Tuberculin is useless. Installations of 10% menthol, orthoform *et cetera* are given several times daily, especially before meals. Alcoholic injections of the superior laryngeal nerve will insure a more lasting anaesthesia. If this effect be not obtained, the nerve can be resected. Circumscribed areas of infiltration should be treated with the electric cautery. In recent years X rays or better still, ultra-violet rays have proved of great value, enabling the patient to be treated at home. The treatment takes at least two or three months and is technically difficult, but well worth while.

#### Essential Hypertension.

H. O. MOSENTHAL (*The Journal of the American Medical Association*, September 8, 1928) discusses the treatment of essential hypertension. Frequently in health the blood pressure is high; in some persons the systolic pressure is from 130 to 160 millimetres of mercury. In these a steady rise of blood pressure does not occur, as in essential hypertension in which condition a high diastolic pressure is of

serious import rather than a high systolic pressure. The aetiology is unknown. In treatment the most important thing is adjustment of the life of the individual. Exercise is indicated where possible; that is, if there is no heart failure. In younger subjects tennis may be played; in older ones golf and walking are advised. As obesity often coexists with high blood pressure of this kind, an attempt to prevent excessive obesity by omission of fats and some carbohydrate is indicated. Proteins should be restricted only when the blood urea content is high. There is no other contraindication. A calm existence with ample rest is advisable. Busy men should cut down their responsibilities. Omission of salt has served no useful purpose in reducing blood pressure. All forms of protein food can be taken. Sodium sulphocyanate and thiocyanate have been lately recommended, but the results are still indecisive. Drastic purgation is ineffective in reducing blood pressure. When the heart begins to fail, digitalis is effective.

#### Relation of Tuberculosis to Pregnancy.

F. SCHULTZE-RHONHOFF (*Klinische Wochenschrift*, October 14, 1928) has reviewed the literature dealing with tuberculosis during pregnancy and has then summarized the opinions of the Heidelberg school. Whenever a tuberculous pregnant woman is seen, a consultation with a physician is arranged and the patient carefully observed over a lengthy period, if necessary. By this means a more correct idea of the extent of the lesion and of the necessary procedure to be taken is obtained than if a decision be reached after a short examination. If the pulmonary lesion be inactive, he advises intensive treatment, preferably in a sanatorium, while the pregnancy is allowed to continue. Patients with definite symptoms of progressive disease, provided that the pregnancy is at least of four months' duration, are treated in a similar manner to those with quiescent lesions. If the pregnancy be not over three months, he still advises non-interference, but admits that there is great difference of opinion in the matter. He maintains that the use of modern methods of treating tuberculosis should yield as good results with the gravid patient as those known to occur with the non-pregnant woman. In conclusion he admits that the last word has not yet been spoken on the subject.

#### Early Diagnosis of Dengue Fever.

M. GEORGOPOULOS (*Münchener Medizinische Wochenschrift*, October 19, 1928) from his experience in the recent epidemic in Greece, discusses the value of two signs in the early diagnosis of dengue fever. The first or Rumpel-Leede phenomenon depends on the appearance of multiple petechiae following the application of a ligature to the arm. The other consists in obtaining a sample of venous blood from the arm, then applying a

firm ligature for twelve minutes and taking a second specimen of blood. Both specimens are kept overnight in an ice chest and a comparison with the refractometer of the sera is made. In addition the percentage of albumin in the blood is tested. Serum from patients in whom damage of the peripheral vascular walls is seen, as in those suffering from dengue fever, manifests an increase as compared with serum from normal vessels. The first sign was found in every case, often on the first day and invariably by the second or third. The number and size of the petechiae varied considerably, but on the whole corresponded with the severity of the attack. The author considers that the Rumpel-Leede sign can be depended upon and, if absent on the second or third day, that dengue can be excluded. It is also obtained with scarlet fever, typhus and malignant endocarditis, but the characteristic symptoms of these diseases will readily lead to their exclusion. The second sign, while of considerable value, is not quite so constant as the former and requires further investigation.

#### Remittent Fever.

N. SJOERSEV (*Deutsche Medizinische Wochenschrift*, November 16, 1928) states that in Denmark cases of remittent fever resembling Malta fever and due to infection by the *Bacillus abortus* of Bang are more common than typhoid or paratyphoid infections. During the past year he has investigated seven and the details of three are given. It is noteworthy that raw milk formed a large part of the diet in all cases. He concludes that the bacillus of Bang can infect the human body and gains access through the drinking of raw milk. The temperature curve shows definite undulations, each wave taking from seven to nine days to rise to a maximum and return to normal. The interval between the curves is usually three days. The general condition of the patient is characteristic as compared with Malta fever in that little alteration in weight occurs and the appetite remains good except at the height of the fever. Occasionally catarrhal symptoms are present, but soon disappear. The blood count is normal and no enlargement of the spleen or cutaneous rashes are noted. The course of the disease is prolonged, but the prognosis is good. The diagnosis was confirmed by agglutination tests, the bacillus of Bang being used as the antigen. In addition the bacillus was recovered from the blood. When an autogenous vaccine was employed the course of the disease seemed to be slightly shortened.

#### Syphilitic Aortitis.

H. SCHLESINGER (*Wiener Medizinische Wochenschrift*, December 15, 1928) states that usually there is an interval of fifteen to twenty years between the original syphilitic infection and the appearance of specific changes in the aorta. Uncomplicated cases affect only the ascending por-

tion of the vessel and lead to a diffuse dilatation. The clinical signs—aortic murmur with accentuation of the second sound, abnormal X ray findings, increased blood pressure and retrosternal pain—make the diagnosis moderately certain except when the blood yields no reaction to the Wassermann test and this occurs in about one-third of the patients. Although some patients' condition remains unchanged without treatment, aortic insufficiency, angina or aneurysm must always be feared. Aortic insufficiency is of slow onset and generally associated with aortic stenosis. Angina may be combined with it or appear alone and, although usually classic in type, may occur in atypical forms with abdominal pain. Syphilitic aortitis was found in 4% of all bodies examined *post mortem* in a large German series. The prognosis is unfavourable. Uncomplicated lesions may remain stationary for long periods, but more than half the patients die from the aortic lesion. The author gives sodium iodide 1.0 to 2.0 grammes *per diem* followed by bismuth or mercurial injections. After this "Neosalvarsan" is used, the initial dose being 0.45 grammes, 3.0 to 3.5 grammes in all being given. This is repeated after an interval of two months. "Stovarsol" is also of value; half, one, one and a half tablets of 0.25 grammes are given on three successive days followed by an interval of three days and then the dose is slowly increased until three tablets daily are given. A course consists of twenty-five tablets (6.5 grammes). At the conclusion sarsaparilla is given for months. Aortic pain soon disappears, pulsations become less pronounced and improvement in the cardiac condition occurs. If, however, cardiac insufficiency be present, no improvement can be expected.

#### Pulmonary Tuberculosis.

LÉON BERNARD (*La Presse Médicale*, November 17, 1928) in his inaugural lecture as professor of tuberculosis in the Paris Faculty of Medicine, pleads for the recognition of pulmonary tuberculosis as a specialty in medicine. After pointing out that specialization in medicine has existed since ancient Egyptian times, he admits that there is a difficulty in defining legitimate specialism. A consideration of the present accepted specialties reveals a diversity of criteria whereby they have become established. After mentioning some of the older ones such as ophthalmology and dermatology, which deal with a certain part of the body, he notes the tendency of certain specialists to take for their scope a single disease by reason of its ubiquity and its clinical, pathological and perhaps social importance. This has been done with syphilis which has in France been divorced from dermatology and now exists as a separate department. In this latter field, the author maintains, the setting of pulmonary tuberculosis as a specialty marks an important advance in

scientific progress. In justification of this assertion he reviews the different chapters in tuberculosis, showing how individualized and characteristic they are, as becomes a specialty. *Ætiology*, with its problems of interrelation between soil and seed, of primary and secondary infections, of mutation of species and ultramicroscopic forms of the "virus," is quite distinct from that in any other infectious disease. In morbid anatomy and clinical phenomena there is a polymorphism which is extraordinary and very puzzling without careful study. In diagnosis modern methods demand a knowledge of radiography and bacteriology in addition to clinical experience which requires intensive training. The treatment of tuberculosis, too, is a large subject. In addition to general and symptomatic treatment there is required a knowledge of chemo-therapy and of operative procedures, particularly artificial pneumothorax which can be acquired only by long experience. Prophylaxis is entirely different to that of any other disease. With its social and veterinary aspects and its dispensary problems none but fully trained and competent physicians can cope successfully. In the new department which Professor Bernard has inaugurated, he proposes to enrol three separate classes. One will be for students who are at present sadly lacking in accurate knowledge of chest diseases and of tuberculosis. The second will be for post-graduates who desire to supplement their knowledge of pulmonary tuberculosis. The third will comprise two courses annually for those desirous of becoming specialists for dispensary or sanatorium practice.

#### The Filterable Elements of the Tubercle Virus.

A. CALMETTE (*Revue de la Tuberculose*, October, 1928) reviews the work that has been done in isolating a filter-passing variant of the tubercle bacillus and in proving the possibility of its infecting the fetus by passage through the placenta. He accepts it as proven that an ultramicroscopic, filter-passing element is present in tuberculous sputum, pus and fluids generally and that it can also be found in the circulating and menstrual blood of tuberculous women. Animal inoculation with these elements does not cause tuberculous lesions, but swelling of the lymphatic glands results and from the lymphatic glands the typical bacillus of Koch has been obtained. Further, these animals become sensitive to tuberculin. Calmette is also satisfied that these ultramicroscopic elements can and frequently do pass through the placenta in pregnant tuberculous women. They do not cause any visible tuberculous lesions in the fetus. Nevertheless, it appears that they do cause the death of the fetus or the new-born infant, but only in exceptional cases does this occur. Death is due here to the toxic properties of the "ultra-virus," the only symptoms being marasmic in type,

occurring in the offspring of tuberculous mothers; no *post mortem* lesion of any disease can be found in the body of fetus or infant which has died in this way.

#### Early Diagnosis of Cerebral Tumours.

A. KRECKE (*Münchener Medizinische Wochenschrift*, November 23, 1928) considers that too many brain tumours are not recognized in the early stages by the general practitioner and that therefore valuable time is lost during which operation may be successful. The earliest symptom is increased intracranial tension, as evidenced by persistent headaches extending over a considerable period. Cerebral vomiting, giddiness and slowing of the pulse form the next group of symptoms. Papillary oedema is an early sign, but it is important to note that at the commencement there is no disturbance of vision. Fits or paralysis may be the first signs of a tumour. Paralysis of individual cranial nerves, especially the third and sixth, are very suspicious and in tumours of the cerebello-pontine angle the eighth may be involved. Disturbance of vision, especially hemianopsia, betokens some tumour pressing on the optic tract. Paralysis of one of the extremities is always highly suspicious of cerebral tumour. Improvement in operative results will occur only when the early signs are noted and the patient handed over to a neurologist for further investigation.

#### Immunity and Allergy in the Pathogenesis of Tuberculosis.

ALLEN K. KRAUSE (*Tubercle*, October, 1928) discusses the interaction of forces which takes place when the tissues of the human body are brought into contact with living tubercle bacilli. Two of these are fixed quantities, namely, inherited constitution and virulence of parasites. A third force, namely, environment, is variable and this he regards as the moulding and directing agency in all chronic and many acute tuberculous infections. With the establishment of an initial infection he postulates two additional tissue attributes which affect the progress of the disease. One, immunity, he defines as an increased specific resistance to tubercle bacilli; the other, allergy, he distinguishes as tissue hypersensitivity to tuberculo-protein which arises with the formation of anatomical tuberculosis. These two phenomena are active within the body as long as the disease, tuberculosis, persists. Immunity which has arisen as the result of a primary infection, modifies a process which would be progressive in a non-immune subject. It becomes part of every tuberculous process, once established, checking in most cases permanently what would otherwise be a rapidly fatal disease. Allergy, he considers, is constantly associated with immunity. The allergic reaction is responsible for most of the symptoms of the disease and there is no question that tuberculosis has its

specific symptomatology. These symptoms, then, are to be considered as expressions of tuberculo-immunity at work, even though life be in jeopardy. Far from being ultrasusceptible, tuberculous babies and savages, Krause asserts, are over-sensitive and over-immune. The fulminating tuberculosis to which they succumb, is an expression of an initial massive dosage, occurring in an allergic and over-immune soil; in short, it is the result of an intense allerge-immune action. In the majority of civilized human beings, allergy and immunity aroused by their initial tuberculous infection are able to hold in abeyance their focal infection when they are subjected to the stresses of an average environment. With an increase in these stresses, however, there is a tendency to focal extension and eruption and even to the acuter forms of tuberculosis. This was well illustrated in the great rise in tuberculosis morbidity in Germany during the war years 1914 to 1918. With the removal of these stresses of environment, the active process, if it be not too far advanced, can once again be lulled into quiescence.

#### Etiology of Leprosy.

EDWARD B. VEDDER (*Philippine Journal of Science*, November, 1928) supports the theory of transmission of leprosy by a biting arthropod. The high incidence of leprosy in certain definitely localized areas appears to indicate that some agency other than actual contact with the infected is necessary for the spread of the disease. In Hawaii, Cape Colony and India it was found that only 4.2%, 4.5% and 5.5% respectively of healthy persons living with lepers became infected, while in Japan and Norway the figure was as low as 2.7%. Doctors and nurses in leprosaria never contract the disease. Only one of numerous attempts at experimental transmission of leprosy has proved successful and in this instance it was later claimed that the patient had come from a leprosy family. It is thus evident that if the disease is transmitted by direct contact, it is only with great difficulty, under very special circumstances and usually only after long and intimate association with an infected person. The author, experimenting with mosquitoes (*Aedes aegypti*) found *Bacillus lepræ* in the gut of 41% of a total of one hundred fed on leprosy lesions. Mosquitoes which had recently fed on tubercles containing many leprosy bacilli, were allowed to bite two healthy prisoners who still showed no signs of the disease in June, 1928, respectively twelve and fourteen months after the inoculation.

#### The Diagnosis of Endemic Yellow Fever.

W. H. HOFFMAN (*American Journal of Tropical Medicine*, November, 1928) discusses the diagnosis of endemic yellow fever. In epidemics the clinical diagnosis of severe yellow fever is usually easy, but the disease

in its endemic form is often mild and recognized only with difficulty. In countries where yellow fever occurs endemically, attention of authorities should be concentrated on local or key places which maintain the infection, and every instance of febrile infectious disease should be investigated by a commission of experts. The author is of the opinion that a positive diagnosis in a suspicious case can best be made by anatomical examination. The histological appearances of the liver in a fatal case cannot be confused with those seen in any other disease presenting similar clinical manifestations. In a non-fatal instance diagnosis should be made by examination of the liver of a monkey inoculated with the blood of the suspected person.

#### The Relation of Plasmodium Falciparum to the Erythrocyte.

HERBERT L. RATCLIFFE (*American Journal of Tropical Medicine*, November, 1928) claims to have proved the generally accepted theory that *Plasmodium falciparum* lives within the red blood cell. Basing their conclusions on a study of blood smears, washed blood cells or cells treated with hypertonic and hypotonic solutions, several observers have expressed the view that *Plasmodium falciparum* does not enter the red cell, but is attracted thereto. The author cut sections of placental tissue of a woman suffering from malignant tertian malaria. The sections were stained with Harris's hamatoxylin and examined microscopically. Microphotographs were taken and camera lucida drawings were made of infected red cells seen in cross-section. The plasmodium was invariably found to be within the erythrocyte.

#### Prevention of Malaria in Kenya.

A. R. PATERSON (*Kenya and East Africa Medical Journal*, November, 1928) discusses the report of the European Malaria Commission to the League of Nations in regard to the applicability to conditions in Kenya of the recommendations of the Commission. The Commission lays stress on the fact that it is concerned with the elucidation of the malaria problem mainly in countries where very expensive works cannot be undertaken on account of lack of funds. The Commission states that those who have used modern methods in the prevention of malaria, have been too apt to aim only at the elimination of anopheline breeding places and in this regard a remark of Robert Koch is brought to mind: "It is beyond human power to destroy or even considerably to reduce a species of insect like the anopheles in large districts." Antianopheline measures, conducted on a large scale, have proved highly satisfactory in various countries, but are by no means universally applicable. The Commission is of the opinion that in countries where the matter of expense is a serious con-

sideration, the greatest degree of success in antimalarial measures is likely to be realized by free issue of quinine, improvement in racial hygiene, education of the masses in the use of quinine and the mosquito net and in the recognition and destruction of the adult anopheles. It has been proved by actual experience that where similar methods have been adopted, a healthy community can flourish in surroundings which were formerly highly malarious and where anopheline mosquitoes abound. Paterson expresses the opinion that the recommendations of the Commission can be applied to a native country such as Kenya, whereas antianopheline measures of sufficient magnitude cannot be undertaken.

#### Tellurium Therapy in Leprosy.

RODALFO STANZIALE (*Journal of Tropical Medicine and Hygiene*, February 1, 1929) describes his experiments with tellurium injections in five cases of leprosy. The drug was used in the following forms: Metallic tellurium (10%) in glucose suspension, biniodide of tellurium (10%) in oily suspension, iodine tellurate of quinine (5%) in oily suspension. The injections which were made into the gluteal muscles, were attended in all save one instance (macular leprosy) with considerable pain, local reaction and rise of temperature to 38.5° C. or 39° C. Four of the patients were suffering from anæsthetic tubercular leprosy and the fifth from macular leprosy. Injections were given at intervals of four to eight days. One tubercular leper had only three injections before leaving the clinic of his own will. In his case some of the tubercles showed signs of regression after the second injection; after the third injection nearly all the tubercles tended to a regressive phase, some becoming softer, smoother and in places almost gelatinous; there was a progressive tendency on the part of the ulcerations to heal. The remaining three tubercular patients were given seven (total of 0.7 gramme), nine (total of 0.7 gramme) and ten (total of 1.0 gramme) injections respectively. In each instance the tubercles tended to regress and soften and the ulcers to heal, though fresh ulcers occasionally appeared during treatment. The patient suffering from macular leprosy was given nine injections, receiving altogether 1.70 grammes of tellurium, with no apparent improvement. In none of the patients was there any immediate alteration in the serological reactions. All the patients became thin and lost weight and emitted a pronounced garlic odour; the skin developed a bluish pigmentation while the hair lost its pigment to some extent. Examination of a regressing tubercle in one of the patients revealed degenerative changes in the bacilli in the leprosy cells. The author admits that it is too early to express an opinion as to the value of tellurium as a therapeutic agent in leprosy.

## British Medical Association News.

### SCIENTIFIC.

A MEETING OF THE NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION in conjunction with the Section of Hygiene and Preventive Medicine and the Section of Pathology and Bacteriology was held at the B.M.A. Building, 30-34, Elizabeth Street, Sydney, on September 27, 1928, Dr. J. E. V. Barling, the President, in the chair.

#### Recent Advances in Immunology.

DR. F. M. BURNET read a paper on the clinical aspects of the bacteriophage (see page 406).

DR. E. L. MORGAN read a paper entitled "Recent Advances in Immunization" (see page 410).

DR. A. H. TEBBUTT, D.S.O., read a paper entitled "Scarlet Fever" (see page 414).

DR. J. S. PURDY, D.S.O., quoted some figures which he held might be of interest to the members. In 1927 the number of cases of scarlet fever notified in the metropolitan area of Sydney was 5,793 which yielded an attack rate of 4.6 per thousand of population. In 1926 the attack rate was 2.07 which was in excess of that of any year since 1916 when the attack rate was 3.24 per thousand of population. The mortality in 1927 was 1.54% as compared with 1.36% in 1926. Dr. Purdy was of the opinion that terminal disinfection was useless in controlling the disease and that isolation did not have the desired effect. He advocated current disinfection of the patient. He had no experience of the Dick test, but had no doubt that in the future immunization would be practised both for scarlet fever and for measles. It was unfortunate that the majority of patients suffering from scarlet fever had to be sent to hospital. In his opinion this course was necessary only when the patients lived in a house from which milk or other food was distributed or when the circumstances were such as to warrant removal for treatment.

DR. C. H. SHEARMAN thanked Dr. Burnet for his most interesting paper. A few years previously interest had centred around the work of Metchnikoff and Ehrlich. It had changed to that of d'Herelle and Besredka. If anyone had the patience to wade through d'Herelle's writings he would have no doubt concerning the importance and reality of the bacteriophage and its therapeutic application. Although Besredka disagreed with d'Herelle in his work of local immunization, he reached a somewhat similar conclusion.

In dealing with the specificity of the streptococci in scarlet fever Dr. Shearman said that every one would agree that the *Streptococcus hemolyticus* had an important bearing on the aetiology. He referred to the recent work of Peters and Allison who had suggested that some other factor was involved. All patients with scarlet fever did not react favourably to streptococcal antiserum. Some became affected with post febrile adenitis and others by phagedæna; the latter condition responded to injections of "Galyt." It would seem that some symbiotic agent was at work. Dr. Shearman referred to the custom which had prevailed a few years previously, of taking swabs from the throats of diphtheria patients and their contacts and of isolating those from whom diphtheria bacilli were obtained. Many who harboured the organism, were not infective, because the organism was non-virulent. There was no possibility of testing for virulence in scarlet fever. He thought that they ought to proceed with caution before adopting the extreme measures in the latter disease which had previously been adopted with diphtheria.

DR. HARVEY SUTTON, O.B.E., thought that Dr. Burnet's contribution was a very important one. He proposed to discuss the other papers, as they were of greater direct interest to him. He referred to the difference in the experience between private schools and public schools in regard to the control of diseases like scarlet fever and diphtheria. It had been noticed in the State school population Schick testing had revealed that there was much less susceptibility towards the disease where it was preva-

lent than where there was little infection. For example in a certain country high school the Schick test of pupils over thirteen from the town where diphtheria was endemic disclosed that the majority was immune, while in pupils from the countryside around where diphtheria occurred only sporadically, the majority was susceptible. The latter group corresponded with the findings in pupils attending the greater public schools. It was very difficult to achieve much in the public school, chiefly because the control should be exercised in the pre-school years. In the great public schools the converse appeared to be the case and yet there was little or no control exercised. In England the majority of the great public schools had full time or part time medical officers. In Australia, however, a few schools had part time medical officers and in general did nothing. Geelong Grammar School was the only school in Australia with a full time school medical officer. He maintained that control was quite possible and attributed much of the blame to the lack of interest in the very schools which were mainly supported by the medical profession and to which medical practitioners sent their own children. The medical profession should put its house in order before it could expect others to do the same. He had been driven to the conclusion that much more control of communicable diseases should be exercised in the home. The general medical practitioner was the first line of defence and it was to him that they should look for assistance. This recommendation had been made by the Royal Commission on Health. He thought that provision made in hospitals for the acceptance of patients suffering from certain infectious diseases was admirable. But even in this regard the private practitioner was the only man able to take the initial steps. He hoped that the papers would arouse the members of the profession to a sense of their responsibility.

DR. MARJORY LITTLE thanked Dr. Burnet for his instructive paper. He was the only man in Australia who was carrying out work in connexion with the bacteriophage. She asked him to give some practical details in connexion with the application of bacteriophage in treatment.

DR. KEITH INGLIS, as the Chairman of the Section of Pathology and Bacteriology, called attention to the fact that Dr. Burnet was there representing the leading medical scientific institution in Australia. They were delighted to have the Assistant Director of the Walter and Eliza Hall Institute to address them. He hoped that movements of this kind would maintain the cordial relationship that existed between the profession in Victoria and New South Wales.

DR. BURNET in reply pointed out the differences between the staphylococcus bacteriophage and the "antivirus" of Besredka, but referred to the views of Broynoghe and others that the same agent, a product of lysis of staphylococci by any means whatever, was responsible for the therapeutic effects of both preparations. Bacteriophage given by the mouth was not influenced by the hydrochloric acid in the stomach and could be isolated in the faeces. If given subcutaneously, it readily attacked foci of infection.

DR. E. L. MORGAN in reply referred to Dr. Tebbutt's remarks concerning returned cases. He stated that the problem had been effectively handled at Aberdeen. All the contact children had been tested by the Dick method and the susceptibles had been immunized. After this had been done no "return cases" had occurred. This was one way in which the general practitioner could help. In regard to the amount of toxin for immunization the dose used by different investigators varied from one unit to sixty thousand units. The best results were obtained with large doses. For immunizing the usual method appeared to be three injections given at intervals of a week in amounts ranging from two hundred and two thousand skin test doses, though sometimes four or five injections usually with a much higher maximum dose were recommended. Satisfactory immunization should result in 90% becoming immune.

DR. A. H. TEBBUTT in reply to Dr. Shearman said that scarlet fever antitoxin was antitoxic and not antibacterial. It was true that the antitoxin did not clear up complica-

tions, in fact it was doubtful whether it prevented them. It was claimed, however, that the antitoxin did have a definite effect in combating the toxæmia, if used early in the disease. He considered that the search for carriers by bacteriological examination of the nose and throat and the use of the Dick test were useful procedures. He referred to the case of a doctor's son who had been removed from school on account of an outbreak of scarlet fever. This boy did not react to the Dick test nor did he contract scarlet fever. His sister did, however, and it was then found that the boy harboured in his nose and throat numerous hæmolytic streptococci of the scarlet fever type.

He agreed with Dr. Harvey Sutton and advocated a full time medical officer and the establishment of pathological and public health laboratories at the great public schools. There was ample work to be done. His time would not be spent looking down drains. He should have special training in the infective diseases and in bacteriology. During epidemic periods there should be a parade of throats every day and the bacteriological examinations should be done immediately on the spot. The pre-school age was undoubtedly important. There should be close cooperation between the general practitioner and bacteriologist. For the children of the poor there should be Government bacteriologists working in conjunction with the general practitioner. Personal contact with the homes of the people as well as with the schools was essential. He did not wish to cast any reflections upon his friend, Dr. Morgan. The latter had not enough men on his staff. More public health men should be trained as bacteriologists. Two scarlet fever and two diphtheria bacteriologists could easily be fully employed in investigating the problems presented by these diseases in the State. He was satisfied that true economy would be effected by the saving of life and the prevention of the permanent damage done by these diseases and their complications. He referred to one school in which there had been sixty cases of scarlet fever. It was a reasonable estimate that each child had cost its parent forty pounds. This made a total of £2,400, the price of a small epidemic of scarlet fever, sufficient to pay the salaries of two bacteriologists for twelve months.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Alfred Hospital, Melbourne, on September 19, 1928. The meeting took the form of a series of demonstrations by members of the honorary staff.

#### Acute Nephritis.

DR. J. P. MAJOR showed a woman, aged thirty-two years, who had been admitted to hospital on September 3, 1928, with a diagnosis of acute nephritis. For three weeks she had vomited every morning before her meal and her ankles had become swollen. There had been no abnormal menstrual, bowel or urinary symptoms. Examination revealed a soft systolic bruit at the cardiac apex beat. No abnormality was detected in the lungs or abdomen, but there was some oedema of the ankles with pitting on pressure. The history given was that she had had fits at intervals of from one to three months for two and a half years. These had become more frequent and were occurring every evening. The patient became unconscious and flaccid, fell down and frothed at the mouth. She had bitten her tongue in one attack. The unconsciousness lasted for five or ten minutes and was followed by a dazed condition for about half an hour. There was no incontinence of urine or feces. She had one son, but had had no other pregnancies. The urine contained hyaline, granular and cellular casts, red blood corpuscles, pus cells and epithelial cells. The blood urea content was 53 milligrammes per hundred cubic centimetres of blood. The urea concentration was 1.2% at the end of the first hour and 1.1% after two hours. The *fundi oculi* were normal.

#### Jacksonian Epilepsy.

Dr. Major's second patient was a labourer aged sixty-eight, who had been admitted on August 13, 1928, with a

diagnosis of subdural hematoma causing Jacksonian epilepsy. On admission he had complained of twitching of the face twenty-four hours before, followed by unconsciousness, lasting about half an hour. Some ten weeks before he had sustained a head injury, with bleeding from the left ear and had fractured seven ribs, for which he had been admitted to hospital. Two days later he had developed twitching of the left side of his face (supranuclear) extending to the right side of his face and at the same time the plantar reflex on the left side had been extensor in type. These signs had improved, leaving temporary right facial paresis. No abnormality of his central nervous system had remained before discharge four weeks later and X rays had revealed no abnormality in his skull.

Since then he had felt well except for an occasional left temporal headache, giddiness and mild insomnia. There had also been some paresis of the left hand since the accident, but no twitching of the face or limbs and no signs of involvement of the speech association areas. His memory was fairly good and his recognition and perception were good. There was no affection of his bowels or bladder.

The day before his second admission to hospital the left side of his face had commenced to twitch and a few minutes later he became unconscious. His breathing had apparently been normal. He had frothed at the mouth, but had not bitten his tongue. These symptoms had lasted for about half an hour after which he had vomited twice and had then felt fairly well. His bowels were regular and his micturition normal. His vision and hearing were becoming impaired.

Examination had revealed no abnormality of his heart, lungs or abdomen. There was a scar in his left temporal region. His reflexes had been all normal and equal. His appreciation of all forms of superficial sensation had been normal, except the volar and dorsal aspect of the left hand and to a less degree of the left forearm. Heat and cold sensation had been impaired most, light touch and pinprick to a less extent. On the motor side there had been paresis of all the small muscles of the left hand and some of the forearm, with very slight wasting of the muscles affected. His cranial nerves had been normal. On August 15, 1928, his left plantar reflex had been extensor. On August 19, 1928, he had had two fits, lasting a few seconds and three minutes respectively. He had remained conscious during the fits which consisted of twitching of the left side of the face and gross movements of the limbs.

On August 22, 1928, his condition had been unchanged. On August 23, 1928, he had had two more fits.

On August 31, 1928, an operation had been performed by Mr. St. Clair Stewart. A flap had been raised to expose the bone over the precentral area. The bone had been removed by trephine, the *dura* opened and a blood cyst found immediately beneath the opening, pressing on, but not in the brain substance. The cyst had been opened and part of the contents removed. A wick drain had been inserted before the wound was closed. On September 3, 1928, the patient had had no headache and no fits, on September 5, 1928, his left plantar reflex had still been extensor. On September 9, 1928, it was equivocal. On September 13, 1928, he had been discharged. His blood serum had failed to cause deviation of complement in the Wassermann test.

#### Pernicious Anæmia.

Dr. Major's third patient was a female, aged sixty-four, suffering from pernicious anæmia.

Her illness had commenced about twenty months before with substernal pain, weakness and dyspnoea. She had later developed extreme anæmia and had been treated for pernicious anæmia with blood transfusion, liver feeding *et cetera*. She had been discharged and had continued with liver feeding for a short time, but had recently become much weaker and unable to walk owing to weakness and stiffness of her knees. Sensation was impaired in her feet and there was occasional tingling in her arm and hand, but no lightning pains. Her vision and other special senses were normal. Her bowels were regular and her

micturition normal. She had had rheumatic fever thirty years before. She had one child alive and well and one had died in early infancy from diarrhoea.

On examination of her heart, there was found to be a systolic bruit at the mitral and aortic regions. Her lungs were normal. Both plantar reflexes were extensor and her ankle jerks absent. All her other reflexes were normal. There was diminished sensibility to pinprick, light touch and heat over the soles of the feet especially the toes. Vibration sensation was absent. Position sense and coordination were fairly good. There was slight stiffness of both legs with paresis of the *quadriceps* and hamstring muscles, but no muscular wasting. Treatment consisted of the administration of four cubic centimetres (one fluid drachm) of diluted hydrochloric acid with meals, 240 grammes (eight ounces) of fresh liver daily with massage and active exercise for her lower limbs.

The patient's improvement was shown by the fact that on September 1, 1928, the power in her legs had begun to increase and ten days later she had been able to walk feebly with the aid of a stick. On September 19, 1928, she had been walking much better. Her blood serum had failed to cause any deviation of complement by the Wassermann test even after a provocative infection of "Novarsenobenzol."

Blood examination in June, 1927, had yielded the following result:

Erythrocytes per cubic millimetre	2,180,000
Leucocytes per cubic millimetre	4,000
Hæmoglobin value	30%
Colour index	0.6

There had been definite anisocytosis and poikilocytosis and a few nucleated red and immature white cells had been seen.

On August 25, 1928, blood examinations had yielded the following information:

Erythrocytes per cubic millimetre	2,000,000
Leucocytes per cubic millimetre	2,200
Hæmoglobin value	43%
Colour index	1.02

There had been anisocytosis and poikilocytosis of red cells; many megalocytes and some macroblasts and normoblasts had been seen.

On September 19, 1928, the finding on blood examination had been as follows:

Erythrocytes per cubic millimetre	4,100,000
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Slight anisocytosis had been seen, but no immature red cells or megalocytes.

At the time of the meeting the patient had much improved as the result of treatment and Freudel's exercises. The plantar reflexes were normal and the ataxia and spasticity were much less noticeable.

#### Acquired Transposition of the Heart.

DR. M. D. SILBERBERG showed a male patient, aged thirty-six years, who was suffering from acquired transposition of the heart and displacement of the trachea. The patient gave a history of having been blown up at the war in 1917 by a shell explosion. He had suffered from right sided pleurisy with effusion in 1918. He had since developed pulmonary and renal tuberculosis. For some years the heart had been completely transposed to the right. The apex beat was in the sixth right intercostal space fifteen centimetres (six inches) from the middle line. The heart sounds were clear and the electrocardiographic tracing was normal.

#### Persistent Right Arm Tremor.

Dr. Silberberg also showed a male patient, aged forty years, who gave a history of having had a vague illness at the war in 1917; he had not been in hospital, but had become depressed and irritable. A movement of the right arm had been noticed in 1920, described by a medical examiner as a tic. He had been admitted to the Alfred Hospital in 1920 complaining of severe frontal headache, vomiting and diplopia. He had been knocked on the head by a horse some days previously. Slight paresis of the

superior oblique and external rectus muscles had been present, but otherwise no abnormality had been detected. On two occasions he had obtained relief from his headache in hospital by the discharge of blood and pus from his nose, evidently from frontal sinusitis. The movement of the right arm had increased after this and had remained in much the same condition for about eight years, though he had done labouring work up to within twelve months of his admission to hospital.

On examination the patient was seen to have a somewhat mask-like face. The pupils, fundi and cranial nerves were normal. There was a constant lateral movement of the right arm which the patient did not control by voluntary effort. The movement had been seen to cease temporarily, but was made worse by excitement. Deep and superficial reflexes were normal, sensation was normal and no reaction had been obtained to the Wassermann test. Various opinions had been expressed that the condition was functional or post-encephalitic. Dr. Silberberg said that he regarded the condition as probably post-encephalitic with a functional element added. He drew attention to the fact that there had been no progress in the condition for eight years.

#### Post-operative Parathyroid Tetany.

Dr. Silberberg's third patient was a female, aged thirty-six years, who for three years had suffered from exophthalmic goitre, and had rapidly become worse with rapid loss of weight and attacks of diarrhoea, cardiac dilatation and tachycardia. The basal metabolic rate had been 50 until her operation in January, 1928. Rapid improvement in nutrition had occurred and the tachycardia had become less. The wound had become infected and a slight keloid condition had developed. Since that time the patient had developed severe attacks of typical tetany. The blood calcium content was low, down to 4.1 milligrammes per hundred cubic centimetres (the normal level was nine to eleven milligrammes). The blood phosphorus content was high, 5.8 milligrammes per hundred cubic centimetres (the normal level was 3.7). She still had a dilated heart and exophthalmic goitre. The basal metabolic rate had been down to -21, but at the time of the meeting was -8. The blood pressure had been low both before and after the operation. She had had two attacks of acute pulmonary oedema and had been treated with large doses of calcium chloride with parathyroid and thyroid extract by mouth. Intravenous injections of calcium chloride had rapidly abolished the tetany. Parathyroid hormone injections had become available and treatment was being initiated with doses of 0.2 cubic centimetre every twelve hours. Dr. Silberberg showed the electrocardiograms and clinical charts of the patient.

#### Encephalitis Lethargica.

DR. G. E. M. SCOTT, acting on behalf of Dr. W. Summons, showed two patients who were suffering from the effects of *encephalitis lethargica*.

The first was a male, aged eighteen years, who had first attended hospital in 1926 on account of chronic osteomyelitis of six months' duration. He had subsequently received the invalid pension on account of this illness. He had presented himself again on March 22, 1928, complaining of shaking which had been present for the previous twelve months or since about the time of his previous discharge from hospital. He had never "seen double," nor had he suffered from any acute illness.

On examination the patient was found to be a fairly well nourished youth with the typical mask-like features of Parkinsonism. The mouth was open, but there was no obvious sialorrhoea. There was a constant coarse tremor of the hands, not very much increased by voluntary movement. Ptosis was evident, but there appeared to be no ocular paralysis. The sphincters were controlled, the mentality was moderately good. The tendon phenomena were equal and active. He was being treated by the administration of hyoscine hydrobromide in doses of 0.6 milligramme (one one-hundredth of a grain) three times a day. He had shown some improvement in his general condition as regards tremor and speech.

The second patient was a male, aged fifty-eight years, married and with three healthy children, who had first attended hospital on August 13, 1928, complaining that he had partially lost the use of his right hand and arm during the previous twelve months. He had been a painter by occupation, but was working as a gardener. He complained of weakness in the legs causing a difficulty in walking and pain occurred in the back when he did any manual work. He suffered from headaches which were frequently nocturnal and accompanied by nausea. He was distressed by the "shaking" of his hands. His appetite was good and he had not lost weight. The bowels were well open. He passed urine twice in the night. He had suffered from enteric fever twenty years previously and from scarlet fever in childhood. Two years previously he had had an attack of influenza and had remained in bed for three days.

On examination he was seen to be fairly well nourished. Generalized light brown pigmentation of the skin was present, but this did not extend to his mucous membranes. The conjunctivæ were clear. There was no abnormality in heart or lungs and the liver and spleen were not enlarged. The systolic blood pressure was 162 and the diastolic pressure 100 millimetres of mercury. The urine was normal. No reaction had occurred to the Wassermann test and the fundi were normal. Typical Parkinsonian mask and rigidity were present with tremor of the head and the tongue. There was no ataxia. The pupils were small and active. The knee jerks were equal and active. The superficial abdominal reflexes were active. The plantar reflex was flexor. There was no ocular palsy. The mentality was good.

Dr. Scott said that the first patient was interesting because there was no history of an acute illness of any kind and because of the improvement under hyoscine.

The second patient gave the history of an attack of influenza, but the age of the patient demanded the consideration of *paralysis agitans* as a cause of the condition. The onset of *paralysis agitans* was rather more insidious. The cause of the pigmentation appeared to be obscure. The blood pressure reading was against Addison's disease and the absence of sugar in the urine against bronze diabetes. There was no history of the administration of arsenic and there were no signs of goitre. It might be noted that there was no response to the Wassermann test. As a blood film had not yet been made, pernicious anæmia could not definitely be excluded.

#### Acute Rheumatism with Temporary Partial Heart Block.

Dr. H. LAWRENCE STOKES, on behalf of Dr. Summons, showed a male patient, aged sixteen years, who had been admitted to hospital in August, 1927, with the history of shifting pains in some of his large joints during the previous six weeks. During this time he had been taking sodium salicylate without any apparent improvement in his condition and a few days before admission typical rheumatic nodules had appeared on his scalp and wrists. The patient's past history was good and there was no rheumatic trouble in the family.

When admitted the boy had not looked very ill. His heart had been normal in size, the sounds regular and no bruits had been audible.

There had been multiple small subcutaneous nodules over most of the superficial tendons around the joints and also a few very large nodules were scattered over the scalp. Nothing else abnormal had been found and the Wassermann test had failed to yield a reaction. An electrocardiograph tracing taken shortly after admission, showed that a condition of partial heart block had been present, the P-R interval being increased to 0.28 of a second.

Several subsequent tracings had been taken during the next few weeks and for a time the P-R interval had been found to be still further increased in length. One tracing showed very well a condition of gradually increasing heart block with a failure of ventricular contraction after each of the longest P-R intervals. The patient had been discharged to the Caulfield Convalescent Hospital a month after being in hospital, feeling and looking very well and at this time his electrocardiographic tracing had been quite normal. All the nodules had disappeared.

The boy had presented himself for examination a few days previously and he stated that during the past year he has been very well. Another cardiac tracing had been taken and again the curves were normal.

#### Auricular Fibrillation.

Dr. Lawrence Stokes also showed for Dr. Summons a boy aged three years and eight months who had been brought to hospital six weeks previously for some minor trouble, chiefly constipation and lack of appetite. The past history was quite normal, except that it had been noticed that his pulse was rapid since birth.

General examination had revealed no abnormality except a soft systolic bruit, heard over the base of the heart. Also his pulse had been found to be grossly irregular. An electrocardiographic tracing taken at this time showed that a condition of auricular fibrillation had been present and also numerous right ventricular extrasystoles. The boy had been given digitalis 0.42 mil (seven minims) three times a day without any effect on the cardiac rhythm. He had then been given quinidine commencing with 0.03 gramme (half a grain) once a day; after three days' time this had been given twice a day. Two days later the child had commenced to vomit and the administration had been reduced again to once a day. During all this time numerous electrocardiographic tracings had been taken and most of these showed typical auricular fibrillation with extrasystoles, as before. On two occasions P waves had seemed to be present, but this apparently normal rhythm had not persisted and the last tracings show that the heart was still fibrillating.

#### Subacute Nephrosis.

Dr. Lawrence Stokes's third patient, shown for Dr. Summons, was a married woman, aged thirty-six years, who had come to the out-patient department two years and four months previously because she had noticed varying puffiness under her eyes and swelling of her ankles during the previous six months. For some time her appetite had been poor and she had been constipated. There had been no urinary trouble. The past history was quite good.

At this time the results of general examination had been normal, except for some œdema of her ankles. The systolic blood pressure had been 110 millimetres of mercury. The urine had contained albumin, but no sugar. The urea one hour after the urea concentration test had been 1.4% and at the second hour, 2.7%. The blood urea was 35 milligrammes per hundred cubic centimetres. The eye fundi had been normal.

She had been constantly observed since this time. After some months her daily excretion of urine had fallen to 568 cubic centimetres (twenty fluid ounces) and she had become more œdematous, but on her urine being made alkaline with citrate of potash the amount had risen to twice that quantity. All this time her urine had contained excessive albumin, but her blood pressure and the results of kidney function tests had remained within normal limits. However, although she was passing a fair amount of urine and there was very little œdema, she had felt that she had no energy.

Ten months previously her basal metabolic rate had been -20% and her blood cholesterol was 400 milligrammes per hundred cubic centimetres. She had then been given thyroid extract 0.12 gramme (two grains) three times a day and the citrate of potash had been discontinued. This treatment had been persisted in for six weeks and, although she had felt better, her daily urine excretion had fallen to under 300 cubic centimetres and she had become very œdematous. Citrate of potash had then been given together with the thyroid extract and at once the daily urine excretion had risen to over a litre and she had continued to improve.

A month previously further investigations had again been carried out. Her basal metabolic rate had risen to +3%, but for the first time her blood urea had been raised, being 54 milligrammes per hundred cubic centimetres, while the percentage of urea in the urea concentration test had been decreased, being 1.2% in the first hour and 0.8% in the second hour. On the other hand the blood

cholesterol was 189 milligrammes per hundred cubic centimetres which figure was within normal limits. Also the systolic blood pressure had risen to 150 millimetres of mercury. The urine still contained excessive albumin and the daily excretion exceeded a litre. During the last two months she had not felt so well, but there had been very little oedema. A remarkable feature about this case was that as soon as the urine became acid the daily excretion at once definitely dropped.

#### Polycythæmia Vera.

DR. J. F. CHAMBERS showed two patients who were suffering from *polycythæmia vera*. The first was a male, aged fifty-five years, who had been ill for four years, complaining of lassitude, loss of memory, irritability, shortness of breath and vague pains in the chest.

On examination the patient was seen to have reddish blue facial congestion with blood-shot conjunctivæ. The systolic blood pressure was 170 and the diastolic pressure 110 millimetres of mercury. The urine contained a trace of albumin. The spleen was seen to extend one finger's breadth below the costal margin. A blood count had yielded the following result:

Erythrocytes, per cubic millimetre	.. 10,000,000
Hæmoglobin value .. .. .	160%
Colour index .. .. .	0.8
Leucocytes, per cubic millimetre	.. 10,000

The second patient was a male, aged sixty-three years, who complained of shortness of breath, of vague pains in the lower part of the chest, of frequency of micturition and of attacks of giddiness. He had suffered from severe epistaxis three months previously.

On examination the patient had a classical appearance. The cardiac apex beat was situated 11.25 centimetres (four and a half inches) to the left of the middle line. The systolic blood pressure was 208 and the diastolic pressure 150 millimetres of mercury. The spleen was not palpable. The urine contained a heavy cloud of albumin. The veins in the fundi were very dilated. The serum had not reacted to the Wassermann test. The erythrocytes had numbered 7,900,000 per cubic millimetre and the hæmoglobin value had been 140%. The lowest figure for erythrocytes and leucocytes respectively after six months' treatment had been 6,300,000 and 25,000 per cubic millimetre.

In discussing the treatment of these patients, Dr. Chambers said that they had been treated during the previous ten months by phenylhydrazine hydrochloride alone; it had been given by mouth in capsules containing 0.05 gramme twice a day. The essential action of the drug was destruction of red blood corpuscles in circulation and was evidenced in a few days by obvious hæmoglobinuria. In one of the present cases this had continued for one month after suspension of treatment. The mode of production of the hæmolytic which could not be reproduced in a test tube, was unknown. As was to be expected, further increases in the size of the spleen occurred in response to the increased blood destruction. For the same reason blood urea, basal metabolic rate and uric acid output rose.

To avoid the cumulative toxic effects on bone marrow, liver and other tissues, treatment should be intermittent. Up to five grammes had been given as an initial course in reported cases, but it was wiser to proceed more cautiously. When the first patient had received 3.5 grammes the blood examination showed that the erythrocytes numbered 4,000,000 per cubic millimetre and that the hæmoglobin value was 90% and the patient had felt for a short time "washed out." Treatment had been suspended for two months' observation and for the first six weeks he had remained perfectly fit. Symptoms, however, had commenced to recur, he had sustained a temporary attack of unconsciousness and hemiparesis and it had been found that the erythrocytes numbered 9,000,000 per cubic millimetre and that the hæmoglobin value was 160%. With resumption of treatment he had continued to improve again. The tendency for some leucoblastic reaction to be present in all these cases was accentuated by phenylhydrazine and a rising white cell count together with appearance in the film of many primitive cells had been held, as had a

return to normal of the red cell count, to constitute an indication for temporary cessation of the treatment. Both his patients had become rapidly aware of the drug's influence, when its maximum benefit for the time being had been attained and when there were indications for renewal. Their feelings in the matter together, if doubt existed, with a blood examination, when a clear urine showed that the total effect from the last course had been obtained, gave adequate information for satisfactory control.

Dr. Chambers concluded that phenylhydrazine hydrochloride was a therapeutic agent superior to any previously adopted in this disease. Under reasonable observation patients had now been maintained at their occupations in comparative comfort for periods ranging up to five years. The procedure was, of course, purely palliative and, except for improving the general efficiency and lessening the liability to vascular accidents, probably did not affect prognosis. As the abnormal cell formation was not appreciably checked, there was no reason to suppose that the ultimate tendency for bone marrow exhaustion would be in any way minimized. It would, however, be interesting to see whether conditions terminating as pernicious or aplastic anaemia could in some degree be controlled at that stage by liver feeding.

#### Congenital Heart Disease.

DR. KINGSLEY NORRIS showed two patients who were suffering from congenital heart disease. The first was a girl, aged twelve years. She had been brought to the hospital because she had never walked. The most obvious abnormality was an intense degree of cyanosis and a pronounced clubbing of the fingers and toes. The heart was slightly enlarged, but auscultation failed to reveal any abnormality. The erythrocytes numbered more than 8,000,000 per cubic millimetre and an electrocardiogram revealed a right heart preponderance. The legs were wasted and there were postural contractures of the knees and feet.

In contrast the second patient, a girl of eleven years, had suffered from increasing disability of the cardiac type during the previous eighteen months. Pallor was pronounced, the heart was greatly dilated and loud double murmurs were present as well as early clubbing of the fingers. The electrocardiogram was normal. There was no history suggestive of rheumatism or of any preceding infectious disease. The patient was afebrile.

Dr. Norris said that both these patients were regarded as suffering from congenital heart disease. The first girl was probably the victim of a ventricular septal lesion, too gross to produce sufficient disturbance in the blood stream to be manifested by bruits or a thrill. The leg condition would probably be amenable to treatment and an opinion was expressed that there was a hopeful outlook for the child as far as walking was concerned. The second girl might be considered to be suffering from rheumatic carditis, except for the slight clubbing which at her age almost certainly indicated a congenital lesion with a subsequent breakdown.

#### Epilepsy.

Dr. Norris also showed two boys, aged twelve years, who were suffering from epilepsy. The first boy had suddenly begun to have seizures of unconsciousness. The seizures had first appeared eighteen months previously, they had been accompanied by slight twitching and had lasted one or two minutes. From the onset these had occurred at intervals varying from ten minutes to an hour. He had previously been perfectly well and there was no history of any nervous disorder in the family. The condition had been diagnosed as pyknolepsy and a good prognosis given. Dr. Norris explained that the sudden onset, the maximum disability being present at once and the frequency of the fits indicated his rare condition which in the absence of any treatment invariably ceased within one or two years. In this instance the fits had suddenly ceased after five months and the boy had been quite well for a period of nearly a year.

In contrast to the last-mentioned patient the other boy had been having increasingly frequent fits for some years. They occurred at intervals of about a month. Otherwise

he seemed quite normal. The face was marked by the characteristic rash of *adenoma sebaceum*, round red papules, symmetrically distributed down the naso-labial fold and the chin. This condition was invariably associated with extensive sclerotic changes in the brain and renal cortex with progressive mental deterioration. The condition was the rare one known as epiloia and frequently described by the late W. A. T. Lind.

#### Diabetic Coma.

Dr. Norris's next patient was a girl, aged nine years, who gave a history that twelve months previously she had been admitted in a state of deep diabetic coma associated with a blood sugar level of 0.46. She had been out of sorts for the previous two weeks and had passed into coma eight hours prior to admission. Two hundred units of "Insulin" had been administered in six hours and a great improvement had resulted. Within three months the patient had seemed perfectly well, had gone to school and had gained weight. She had continued for three months without "Insulin," but following a mild cold glycosuria had reappeared and since then "Insulin" had been given. At the time of the meeting she was on a liberal diet, was receiving four units of "Insulin" twice a day, was going to school, was gaining weight and appeared to be perfectly well.

Dr. Norris said that this was his second patient with diabetic coma who had achieved freedom from "Insulin" within a few months. Each patient later, however, following a mild infection had been compelled to resort to small doses of "Insulin." "Insulin" had given these patients a ray of hope, when previously their condition had had a fatal termination.

#### Non-tuberculous Pulmonary Lesions.

Dr. Norris also showed two patients who were suffering from chronic non-tuberculous pulmonary infections. "Lipiodol" had been injected by the crico-thyroid route. One patient had an extensive lesion at the left base, following a severe and protracted pertussis. "Lipiodol" had not revealed any bronchiectatic cavity, but following the injection the improvement had been dramatic, the cough had ceased and the boy had rapidly gained in weight. In the other boy, aged twelve years, "Lipiodol" had revealed a bronchiectatic cavity at the right apex. Repeated investigations for a tuberculous infection had all proved useless. The child was being treated by posture, creosote and exercises.

#### Branchial Defects.

Dr. Norris showed a patient who presented multiple branchial defects, numerous accessory auricles, a macrostoma and a branchial cyst in the neck.

#### Trapezial Tic.

Dr. Norris also showed two patients who were suffering from tic involving the cervical portion of the trapezius muscle. Attention to the nose and throat and teeth, sedatives and injection of the accessory nerve had all failed to bring about more than a mild temporary improvement. Continual blistering for six weeks over the affected portion of the muscles had certainly lessened the twitching in one instance and apparently it had effected a cure in the other.

#### Parotitis.

Dr. Norris's last patient was suffering from intermittent, non-infectious, febrile parotitis. No obstruction to the duct could be demonstrated.

#### Asthma.

Dr. CHARLES SUTHERLAND showed four patients who manifested hypersensitiveness. The first was a farmer, aged fifty-eight, who had suffered from asthma for forty years. He noticed that if he handled old bags or chaff, he would be seized with sneezing and rhinorrhoea and asthma would ensue. Skin tests with chaff dust yielded no reaction, but there had been a definite reaction to mouse hair. He had already greatly improved, although he had had only three weeks of treatment.

The next patient was a woman of twenty-nine years who had had attacks of asthma all her life. She noticed that making beds or dusting the house always upset her. She showed definite reactions to feathers of various sorts and to house dust. A large number of other tests had yielded no reaction. She had been instructed to avoid feathers and dust as much as possible and was also having specific treatment with increasing doses of a mixture of the extracts of feathers and house dust and was definitely better.

The next patient had had asthmatic attacks all her life and recently had applied for the invalid pension on account of continuous asthma. When first seen she had been extremely debilitated and had had severe asthma which was completely relieved for a short time by a subcutaneous injection of ten minims of adrenalin solution (one in one thousand). She had been found to have extensively infected sinuses. Skin tests had yielded definite reactions to horse hair, rabbit fur and orris root and she had very definitely improved with specific treatment with the extracts of these substances. The nose condition would be dealt with as soon as she was fit for it.

The next patient suffered from hay fever each year from September to January. He was always free of symptoms when at sea and usually if there was a south wind. He gave skin reactions to the pollens of rye grass, prairie grass, cocksfoot and kangaroo grass. Specific treatment with pollen extract had only just commenced. Each year he would require about fifteen injections before the pollen season commenced. Treatment during the pollen season was seldom as effective.

Methods of testing for hypersensitiveness were demonstrated on each patient and the set of reagents for investigation of such conditions was shown.

#### Diverticulum of the Bladder.

Mr. R. C. BROWN showed a patient who had been operated on for diverticulum of the bladder. An account of this case will be published in a subsequent issue.

#### Carcinoma of the Stomach.

Mr. Brown also showed a man, aged forty-seven years, a plumber, who had been operated on in November 21, 1921, for carcinoma of the stomach. The anterior Pólya operation had been performed and the growth had been a large one. The patient, at the time forty years of age, had been much emaciated and the projecting lump had been visible on the skin surface. The growth had been adherent to the liver and pancreas. After operation the patient had gained 18.9 kilograms (three stone) in weight and he had supported his family by regular work for the last seven years. The patient's weight at the time of the meeting was 80.5 kilograms (twenty stone eleven pounds). Examination of a microphotograph of a section revealed wide invasion and destruction of the muscle layers and colloid degeneration.

Mr. Brown's last patient was a man, aged sixty-five years, who had been operated on for carcinoma of the stomach in July, 1916. The Billroth II operation and transverse colectomy had been performed. The growth had obstructed the pylorus and had involved the transverse colon. The patient had subsequently developed an empyema which had been drained. The patient had earned his living for twelve years, but recently the growth had recurred and signs of liver metastases with ascites were present.

#### Carcinoma of the Rectum.

Mr. Fay Maclure showed a male patient, aged thirty-six years, who had complained in October, 1924, of bleeding from the rectum, followed by diarrhoea and incontinence of faeces. No obstructive symptoms had been present. Rectal examination had revealed a carcinomatous ulcer five centimetres (two inches) above the anus. On October 18, 1924, laparotomy had revealed that there were no secondary deposits in the liver or glands and that the tumour was freely movable. On November 1, 1924, perineal excision of the rectum had been carried out and about fifteen centimetres (six inches) removed; the sphincter had

been reconstituted. The result of the operation had been an apparent cure and the patient had been shown at the Branch meeting in 1925. He had remained well until January, 1927, when constipation and difficulty in defecation had occurred and a recurrent carcinoma at the anus had been discovered. On February 2, 1927, the first stage of Coffey's operation had been performed and nine days later the second stage. Since then the patient had appeared to be quite well. He conducted a poultry farm and played the trombone in a suburban band. He had no trouble with his colostomy.

Mr. MacIure's second patient was a man, aged sixty years, who had come in September, 1927, complaining that three months before that date he had thought that he was suffering from piles; then blood had appeared and he had experienced a frequent desire for bowel action. On rectal examination there had been found a large hard craggy mass in the rectal wall 7.5 centimetres (three inches) above the anus, not involving the prostate, but beginning to become fixed to the pelvic wall. On October 6, 1927, the first stage of Coffey's operation had been performed. The growth had been movable, but the glands in the hollow of the sacrum had been found infiltrated with columnar celled carcinoma. Ten days later the second stage of Coffey's operation had been performed and since that time the patient had been very well.

#### Carcinoma of the Tongue.

Mr. Balcombe Quick showed a series of patients to illustrate the results of surgical operation in the treatment of extensive cancer of the tongue. An account of this will be published in a subsequent issue.

#### Plastic Operation for Cleft Palate.

Mr. Quick also showed a patient, aged seventeen years, on whom he was carrying out a series of operations for cleft palate involving the soft and three-quarters to four-fifths of the hard palate. The septum was strictly mesial and ill-developed. The anterior end of the cleft was bluntly rounded. The pitch of the arch was quite reasonably good, but the cleft generally had not appeared to lend itself to closure by approximation.

Mr. Quick described the stages of his operation:

1. A pedicle tube-graft had been raised from the side of the neck, about 12.5 centimetres (five inches) in length, the lower attachment being just below the clavicle.
2. The upper end had been detached and implanted into the inner surface of the lower lip on the left side.
3. An epithelial inlay had been introduced by a deep incision across the front of the lower attachment, as this portion had been planned to form the middle portion of the soft palate.
4. The lower end of the tube had been detached and after lateral incision and paring of edges sutured in position in the cleft. It had been found that the tube lay better in relation to the palate when passing from behind forwards, then from before backwards. Thus stage 3 had been wasted.
5. Union of the right margin having been obtained, it had been found an impossibility to obtain working room in the mouth until the pedicle was detached from the lip.
6. The pedicle had been detached, the graft had been sutured to the left margin of the cleft.

No attempt had been made to fill the anterior portion of the cleft in the hard palate for which a denture would be fitted. Not until shrinkage of graft had become complete, would any final trimming down be done.

#### Tumour of the Skull.

Mr. Quick also showed a man, aged seventy-seven years, who six months previously had incurred a very slight injury to the head (a bump getting into a car). Since then a slowly increasing swelling had been noticed in the region involved (left fronto-parietal). No pain nor headache had occurred, the general health was excellent, except for trouble with left knee due to an accident many years

before. For the previous seven years the knee had pained him and he thought there had been an increasing deformity there.

Examination had revealed a rounded pulsating and expansile swelling about 6.75 centimetres (two and a half inches) in diameter. The skull underlying this had been deficient. The bone edge had been fairly regular and gave the impression of slight eversion. Compression of the swelling, almost to point of obliteration, had produced no headache; there had been very slight tenderness at one point. Compression of the temporal arteries had diminished pulsation slightly.

On August 24, 1928, X ray examination of the skull had revealed a large area of bone destruction circular in shape; minute remnants of bone in the destroyed area still remained. A small area of periostitis had been found on the posterior surface of the femur in its upper one-third. Very extensive osteoarthritic changes had been present in the left knee-joint and to a lesser extent in hip-joint. Examination of thyreoid and prostate glands had revealed no abnormality.

At operation on August 29, 1928, an incision had been made around rather less than half the circumference of the swelling posteriorly. There had been slightly increased vascularity of the scalp which had been dissected up without difficulty. Bipolar diathermy had been applied with button electrodes on opposite sides of the portion of the tumour exposed. The flap had been sutured. Definite hardening and shrinkage of the posterior portion of the swelling had followed this treatment, which it is proposed to repeat over the anterior part of the swelling.

#### Surgical Treatment of Osteitis Deformans.

Mr. A. J. TRINCA showed four patients suffering from *osteitis deformans*. He discussed the healing of fractures in this condition and described an operation which he had performed on one patient. This report will be published in a subsequent issue.

#### Bilateral Congenital Deformity of Radius and Ulna.

Mr. Trinca also showed a young woman, aged seventeen years, who had fallen on her right elbow and next day had reported to hospital, complaining of pain and disability in the joint. On examination, the soft tissues around the joint had been bruised and swollen. Flexion and extension had been present but painful and the movements of pronation and supination absent. The conclusion had therefore formed that a serious bone injury had occurred, resulting in the loss of these movements. The patient had then volunteered the information that both forearms had been involved for as long as she could remember in loss of the movements of pronation and supination.

X ray examination showed a bilateral congenital deformity in the shape of a sinostosis at the upper end of the radius and ulna. Mr. Trinca said that this deformity was said to be commonly associated with other defects in the bones of the forearm, but in her case this seemed to be the only abnormality present.

#### Cardiospasm.

Mr. Trinca's last patient was a man, aged thirty-eight years, who had come on March 23, 1928, complaining that for twelve months he had had difficulty in ingesting food. A few minutes up to an hour later he had vomited unchanged food. Occasionally he had felt that he could force it through with pain and discomfort into the stomach. He had lost 25.2 kilograms (fifty-six pounds) in weight in sixteen months. On admission his weight had been 53.5 kilograms (eight stone seven pounds). The patient had been in bed for six months in hospital and under treatment by dilatation seven or eight times without any improvement.

On examination the patient had been very weak and wasted. X ray examination had revealed well marked cardiospasm.

On April 16, 1928, gastrotomy and manual dilatation of the cardiac orifice up to four fingers had been performed. For twelve days prior to operation the patient had been treated by daily irrigation of his oesophagus and fed on

sterile fluids in an attempt to render the mucosa of the œsophagus as sterile as possible. It was well known that in this operation there was a risk of mediastinal sepsis following dilatation.

The subsequent history had been one of continued improvement. His weight on August 20, 1928, had been 68.4 kilograms (ten stone twelve pounds), a gain of thirteen kilograms (twenty-nine pounds) in four months. He could eat an ordinary meal without discomfort. X ray examinations since operation revealed a lessening of the dilatation and an almost normal emptying of the œsophagus.

#### Myeloma of the Tibia.

Mr. H. C. COLVILLE showed a girl, aged eleven years, who had been operated on in June, 1927, for a rapidly growing myeloma of the head of the right tibia. At operation the growth had been removed piecemeal and the gap in the bone had been bridged by a sliding bone-graft taken from the tibial shaft. This patient had been shown at the corresponding meeting in 1927, at which time portion of the overlying skin had sloughed exposing the bone-graft and some degree of infection had been present. The exposed portion of the graft had been removed in December, 1927, and from that time healing and bone regeneration had proceeded uneventfully. At the time of the meeting the child had a perfectly sound leg and was able to walk and run without disability.

#### Stricture of the Œsophagus.

Mr. Colville also showed a boy, aged six years, who had swallowed caustic soda solution in July, 1927. When first seen in December, 1927, there had been gross dysphagia from stricture of the œsophagus and rapid loss of weight. Gastrostomy had been performed on December 15, 1927, and thereafter several attempts had been made by Dr. A. Blaubaum to pass a bougie through the stricture by means of the œsophagoscope, but without success. On May 31, 1928, Mr. Colville and Dr. Blaubaum, operating simultaneously, had succeeded in passing a bougie through the stricture from below upwards through the stomach and in bringing it out of the mouth by the œsophagoscope; by this means a silk thread had been passed through the œsophagus and the two ends united externally. Subsequently rubber dilators had been pulled through the stricture once a week from below upwards by means of the thread after the method of Gabriel Tucker, the thread remaining *in situ* between dilatations with its upper end brought through the nose and attached to the cheek by adhesive strapping. At the time of showing the œsophagus had been dilated to size 12 (English) and the child was swallowing soft foods without difficulty.

#### Deformity of the Forearm After Fracture.

Mr. Colville's last patient was a boy, aged twelve, who four months previously had had an injury to the left forearm which had been treated as a sprain. When he was first seen two months later, X ray examination had revealed an old fracture of the shaft of the radius which had united in malposition with the lower fragment fully pronated, so that supination of the hand was impossible. At operation on July 26, 1928, the radius had been sawn through at the site of the old fracture and the hand rotated into full supination; this position had been maintained by inserting a threepenny piece into saw cuts made in the divided ends of the bone. At the time of showing good union had occurred and full supination could be performed without difficulty.

#### Electro-Therapy and Radiation Therapy in Gynæcology.

Dr. ROBERT FOWLER, with the assistance of Dr. C. S. Wood, Dr. R. Douglas Aitchison, Dr. V. Brenton, Dr. Isaac Yoffa and Dr. A. R. Buchanan, gave a comprehensive demonstration of the applicability of electrical and radiant energy to gynæcology.

The methods used were diathermy, ionization, ultra-violet radiation, X radiation and radium emanations. After a few preliminary remarks upon the theoretical relationship of all forms of radiant energy, the demonstrator and

his assistants proceeded to show visitors the clinical assemblage and operation of the necessary apparatus much of which had been kindly lent for the occasion by Hospital Electrical and Radium Limited.

Three patients suitable for surgical diathermy were then submitted to operation. They suffered respectively from a large "target-erosion," a Skene's folliculitis and venereal warts. In the first patient radial linear cauterization with the "cold cautery" was practised, in the second electro-coagulation (a condenser-pad arrangement being used), in the third electro-desiccation with the Oudin monopolar current.

The next series of patients presented conditions suitable for medical diathermy, namely primary dysmenorrhœa, chronic pelvic inflammatory lesions and rheumatoid arthritis of endocervical origin. Vaginal, endo-cervical and external electrodes were used and the appropriate procedures were demonstrated.

Zinc ionization was used for a patient with subacute endocervicitis.

Local and general actinotherapy was then illustrated in patients with *pruritus vulvæ*, non-specific vulvo-vaginitis, post-operative asthenia and the debility of pregnancy. Attention was drawn to the diagnostic value of ultra-violet illumination in visualizing indistinct cutaneous lesions of the vulvar region and also its forensic value by virtue of the characteristic fluorescence exhibited by seminal stains.

Dr. Fowler next applied superficial X radiation to a lichenoid condition of the perineum. Several patients were presented who had been cured of similar conditions by previous exposure to X rays.

Examples of post-operative deep X radiation were then presented, namely, a patient who had undergone excision of the vulva and inguinal glands for epithelioma of the labium; a patient who had been submitted to Wertheim's operation for carcinoma of the cervix; a patient with tuberculous salpingitis and peritonitis.

Finally an exhibit of gynæcological radium applicators was displayed together with the instrumentarium used for their introduction. It was stated that radium therapy was useful in selected cases of *carcinoma cervicis*, myomatosis and *fibrosis uteri*. Dr. Fowler illustrated by reference to unique anatomical preparations the appropriate regional distribution of radium tubes and needles together with the technique of their application in gynæcological conditions.

Dr. Fowler admitted that the demonstration consisted of more or less "novelties" but disclaimed any imputation of "stunting." The therapeutic agencies discussed were standardized in some respects, whereas in others they were undergoing trial. In all cases, however, the methods were worthy and warranted on both theoretical and practical grounds.

### Obituary.

HUGH LATHROP MURRAY.

WE regret to announce the death of Dr. Hugh Lathrop Murray which occurred at Melbourne on March 17, 1929.

### Corrigendum.

PROFESSOR FRANK C. WILKINSON has called our attention to the misplacement of several of the legends to the illustrations of his article, "Oral Sepsis and General Health: Clinical Aspect," which appeared in THE MEDICAL JOURNAL OF AUSTRALIA of February 23, 1929, on page 231. The legend labelled IX belongs to Figure V; that labelled X belongs to Figure VI; that labelled XI belongs to Figure VII; that labelled XII belongs to Figure VIII; that labelled VI belongs to Figure IX; that labelled VII belongs to Figure X; that labelled V belongs to Figure XI; that labelled VIII belongs to Figure XII.

## Books Received.

- ANTE-NATAL CARE: A PRACTICAL HANDBOOK OF ANTE-NATAL CARE AND OF THE ABNORMALITIES ASSOCIATED WITH PREGNANCY**, by W. F. T. Haultain, O.B.E., M.C., B.A., M.B. (Camb.), F.R.C.S.E. and E. Chalmers Fahmy, M.B. (Edin.), F.R.C.S.E., with Foreword by Professor R. W. Johnstone, C.B.E., M.A., M.D., F.R.C.S.E.; 1929. Edinburgh: E. and S. Livingstone. Crown 8vo., pp. 125. Price: 5s. net.
- ESSENTIALS OF INFANT FEEDING**, by E. A. Barton; Second Edition; 1929. London: H. K. Lewis and Company, Limited. Crown 8vo., pp. 88. Price: 3s. 6d. net.
- ON NEPHRITIS (FOR THE STUDENT AND PRACTITIONER)**, by A. Cecil Alport, M.D. (Edin.), M.R.C.P. (London), with an Introduction by Professor Frederick Langmead, M.D., F.R.C.P.; 1929. William Heinemann (Medical Books) Limited. Crown 8vo., pp. 190. Price: 7s. 6d. net.

## Diary for the Month.

- APRIL 2.—Eye, Ear, Nose and Throat Section, South Australian Branch, B.M.A.: Branch.
- APRIL 3.—Victorian Branch, B.M.A.: Branch.
- APRIL 3.—Western Australian Branch, B.M.A.: Council.
- APRIL 4.—South Australian Branch, B.M.A.: Council.
- APRIL 5.—Queensland Branch, B.M.A.: Branch.
- APRIL 9.—Tasmanian Branch, B.M.A.: Branch.
- APRIL 9.—New South Wales Branch, B.M.A.: Ethics Committee.
- APRIL 10.—Federal Committee of the B.M.A. in Australia.
- APRIL 10.—Central Northern Medical Association, New South Wales.
- APRIL 11.—Victorian Branch, B.M.A.: Council.
- APRIL 11.—New South Wales Branch, B.M.A.: Clinical Meeting.

## Medical Appointments.

Dr. Henry Laurence Tooth (B.M.A.) has been appointed a Medical Officer, Office of the Director-General of Public Health, New South Wales, on probation for six months.

Dr. Elma Linton Sandford Morgan (B.M.A.) has been appointed a Medical Officer, Office of the Director-General of Public Health, New South Wales, on probation for twelve months.

His Excellency the Governor of South Australia in Council has been pleased to appoint Dr. Douglas Lewis Barlow (B.M.A.) an Honorary Commissioner to inquire into and report upon the recent advances in medical diagnosis and treatment in Great Britain and the continent of Europe.

## Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, locum tenentes sought, etc., see "Advertiser," page xvi.

**DAYLESFORD DISTRICT HOSPITAL:** Resident Medical Officer.

**JANEFIELD SANATORIUM, BUNDOORA, VICTORIA:** Resident Medical Officer.

**LAUNCESTON PUBLIC HOSPITAL:** Junior Resident Medical Officer.

**MENTAL DISEASES HOSPITAL, NEW NORFOLK, TASMANIA:** Assistant Medical Officer.

**NEWCASTLE HOSPITAL:** Resident Radiologist.

**NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION:** Medical Secretary.

**ROYAL NORTH SHORE HOSPITAL OF SYDNEY:** Honorary Vacancies.

**SYDNEY HOSPITAL, SYDNEY:** Honorary Vacancies.

**THE BRISBANE AND SOUTH COAST HOSPITALS BOARD:** Resident Medical Officer.

**THE CHILDREN'S HOSPITAL, INCORPORATED, PERTH, WESTERN AUSTRALIA:** Junior Resident Medical Officers.

**THE UNIVERSITY OF MELBOURNE:** Chair of Obstetrics.

**VICTORIAN EYE AND EAR HOSPITAL:** Resident Surgeons (three vacancies).

**WOMEN'S HOSPITAL, CROWN STREET, SYDNEY:** Junior Resident Medical Officer.

## Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmalm United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company, Limited. Phoenix Mutual Provident Society.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	Members accepting appointments as medical officers of country hospitals in Queensland are advised to submit a copy of their agreement to the Council before signing. Brisbane United Friendly Society Institute. Stannary Hills Hospital. Boonah District Hospital.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	All Contract Practice Appointments in South Australia. Booleroo Centre Medical Club.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Contract Practice Appointments in Western Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	Friendly Society Lodges, Wellington, New Zealand.
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington.	

Medical practitioners are requested not to apply for appointments to position at the Hobart General Hospital, Tasmania, without first having communicated with the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales.

## Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, Sydney. (Telephones: MW 2651-2.)

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